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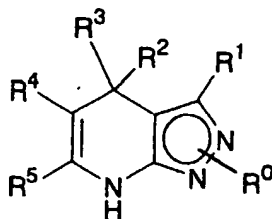
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(54) Title: DIHYDROPYRAZOLOPYRIDINE COMPOUNDS AND PHARMACEUTICAL USE THEREOF



(1)

(57) Abstract: The present invention provides dihydropyrazolopyridine compounds represented by the formula (I): wherein each symbol is as defined in the specification, optically active forms thereof, and pharmaceutically acceptable salts thereof and hydrates thereof. The compounds of the present invention show a selective and strong inhibitory activity on glycogen synthase kinase-3 beta (GSK-3β), and are useful as medicaments for prevention and/or treatment of diabetes, diabetic complications and neurodegenerative diseases or as immunopotentiators.

DESCRIPTION**DIHYDROPYRAZOLOPYRIDINE COMPOUNDS AND PHARMACEUTICAL USE
THEREOF****Technical field**

5 The present invention relates to new compounds for medicaments, which have a glycogen synthase kinase-3 beta (GSK-3 β)-inhibitory activity, and use thereof.

Background art

 It has been reported that glycogen synthase kinase-3
10 beta (GSK-3 β), a protein kinase, is involved in the causes of various diseases as noted in the following.

 Type-II diabetes is a disease in which the insulin reactivity of pancreatic β cells becomes low and glucose in blood increases. As a result, complications such as diabetic
15 nephropathy, retinosis, heart disease and the like are induced. GSK-3 β acts for inhibiting glycogen accumulation in peripheral tissues, lowering insulin response and increasing glucose in blood by phosphorylating glycogen synthase. Lithium having a GSK-3 β -inhibitory activity actually lowers glucose in blood by
20 a GSK-3 β -inhibitory activity (Proc. Nat. Acad. Sci, 93, 8455 (1996)). Therefore, medicaments having a GSK-3 β -inhibitory activity are considered to be a pharmaceutical agent effective for the improvement of Type II diabetes and complications thereof.

25 The developmental mechanism of Alzheimer's dementia has not yet been elucidated. However, it is considered that amyloid aggregation and neurofibril changes are closely related to the cause of the development. GSK-3 β is involved in both the amyloid aggregation and the neurofibril changes as
30 follows. (1) It binds with variant presenilin and increase production of insoluble amyloid (Proc. Nat. Acad. Sci., 95, 9637 (1998)). (2) It causes phosphorylation of the Tau protein, which causes neurofibril changes, and weakens the backbones of

neurons to induce neuronal death (Neurosci. Lett., 128, 195 (1991)). In addition to the above, (3) the direct involvement of GSK-3 β in neuronal death through inactivation of pyruvate dehydrogenase by phosphorylation to decrease the production
5 amount of acetylcholine necessary for maintaining cell activity (Proc. Nat. Acad. Sci., 93, 2719 (1996)) has been reported.

In addition, the effectiveness for AIDS encephalopathia as a neurodegenerative disease other than Alzheimer has been
10 suggested. Tat, which is a protein produced by HIV virus that causes AIDS, enhances GSK-3 β activity in neurons to induce neuronal death (J. Neurochem., 73, 578 (1999)). From the above, GSK-3 β inhibitors are considered to be medicaments effective for improving neurodegenerative diseases including Alzheimer's
15 dementia.

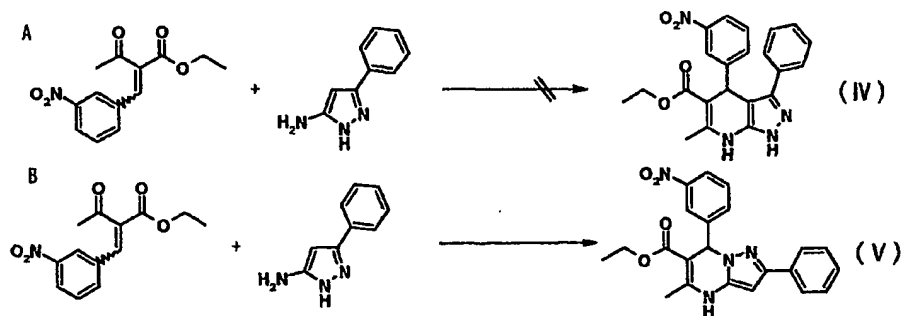
Lithium and valproic acid, which have anti-manic-depressive activity, have a GSK-3 β inhibitory activity (J. Neurochem., 72, 1327 (1999)). The relationship between anti-manic-depressive activity and GSK-3 β inhibitory activity is
20 unclear, but a suppressive activity on glutamic acid toxicity is considered to be partly responsible for maintaining neuronal activity (Proc. Nat. Acad. Sci., 95, 2642 (1998)). Based on the foregoing, GSK-3 β inhibitors are considered to be medicaments effective for improving manic-depressive psychosis.

25 NF-AT, a transcription factor, is dephosphorylated by calcineurin to increase immunological responses (Science, 275, 1930 (1997)). GSK-3 β acts for suppressing immunological function by conversely phosphorylating NF-AT. Therefore, GSK-3 β inhibitors are considered to be medicaments effective for
30 immunopotentialiation.

Incidentally, JP-A-3-272189 (invention drawn to an improved synthesis method of mevalolacton intermediates), JP-A-2-275878 (therapeutic agents for hyperlipoproteinemia and

atherosclerosis) and JP-A-1-272584 (therapeutic agents for hyperlipoproteinemia) disclose pyrazolo[3,4-b]pyridine compounds wherein the 6-position is either methyl, isopropyl or cyclopropyl. These publications do not disclose or suggest
5 any action of these compounds on GSK-3 β or the central nervous system.

The specifications of JP-A-59-65089, JP-A-59-118786, JP-A-60-56979, JP-A-60-197685 and the like disclose 6-methyl-4-substituted phenyl-4,7-dihydropyrazolo[3,4-b]pyridine-5-
10 carboxylate compounds used for the treatment of cardiovascular diseases, and they are produced by similar methods. The present inventors reproduced the following reaction A according to the method described in JP-A-59-65089, but failed to obtain the compound of Example 14 (formula (IV) in the
15 following) described therein. They confirmed that only the pyrazolo[1,5-a]pyrimidine derivative represented by the formula (V) could be produced. They measured IR, NMR and the melting point of the compound of the formula (V) and found them to be identical with IR, NMR and the melting point
20 described in the specification of this publication. It is therefore concluded that an erroneous structural formula has been disclosed in these publications. In other words, 6-methyl-4-substituted phenyl-4,7-dihydropyrazolo[3,4-b]pyridine-5-carboxylate cannot be synthesized according to
25 the methods described in these publications.



The compound of the above formula (IV) can be

synthesized according to the method described in J. Chem. Soc., Perkin Trans. 1, 947 (1996), and this publication discloses methyl 4-(2-chlorophenyl)-6-methyl-4,7-dihydro-1H-pyrazolo[3,4-b]pyridine-5-carboxylate and the like.

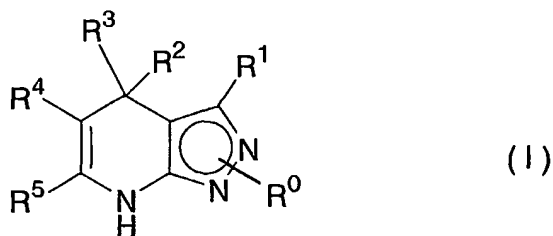
5 Disclosure of the invention

An object of the present invention is to provide novel compounds having a selective and strong inhibitory activity against glycogen synthase kinase-3 beta (GSK-3 β), and further, medicaments comprising them.

10 The present inventors have intensively studied to achieve the above object, and have found that 4,7-dihydropyrazolo[3,4-b]pyridine derivatives have a selective and strong inhibitory activity on GSK-3 β , which resulted in the completion of the present invention. That is, the present
15 invention relates to medicaments comprising, as an active ingredient, dihydropyrazolopyridine compounds represented by the following formula (I), which have a GSK-3 β -inhibitory activity and can be used as medicaments, optical isomers thereof, pharmaceutically acceptable salts thereof, or
20 hydrates thereof.

The present invention provides the following.

1. A dihydropyrazolopyridine compound of the formula (I):



25 wherein

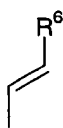
R⁰ is hydrogen, alkyl, acyl, cycloalkyl, formyl, haloalkyl, aminoalkyl, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, aminocarbonyl, alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl, alkylsulfinyl,

alkylsulfonyl, phenylsulfonyl, mercaptoalkyl,
alkylthioalkyl, acyloxyacetyl, acyloxyalkyl, phenyl
optionally having substituent(s), aromatic
heterocyclic group optionally having substituent(s),
5 phenylalkyl optionally having substituent(s), or a
group of the formula: $-COOR^8$ (wherein R^8 is hydrogen,
alkyl, aryl optionally having substituent(s) or
aralkyl optionally having substituent(s));

R^1 and R^2 are the same or different and each is hydrogen, alkyl,
10 acyl, cycloalkyl, hydroxy, thiol, halogen, amino,
formyl, carboxy, cyano, nitro, alkylthio, haloalkyl,
aminoalkyl, acylamino, alkoxy, cycloalkoxy, phenoxy,
phenylalkoxy, aminoalkoxy, alkoxyalkyl, phenoxyalkyl,
hydroxyalkyl, alkoxycarbonyl, aminocarbonyl,
15 alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl,
phenylthio, alkylsulfinyl, alkylsulfonyl,
phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, phenyl
optionally having substituent(s), aromatic
heterocyclic group or phenylalkyl;

20 R^3 is
(1) alkyl or haloalkyl,
(2) cycloalkyl,
(3) phenyl optionally having substituent(s),
(4) aromatic heterocyclic group,
25 (5) a group derived from a benzene ring fused with a
saturated or unsaturated 5 or 6 membered carbocyclic
ring,
(6) a group derived from a benzene ring fused with a
saturated or unsaturated 5 to 7 membered carbocyclic
30 ring containing 1 to 3 heteroatom(s), or
(7) a group derived from a 5 to 7 membered saturated
or unsaturated carbocyclic ring containing 1 to 3
heteroatom(s), which is fused with a benzene ring,

wherein the groups of (2) to (7) may have one or more substituent(s), or a group selected from the groups represented by the following formulas (II) and (III),



(II)



(III)

wherein R^6 and R^7 are each phenyl optionally having substituent(s) or an aromatic heterocyclic group, or R^2 and R^3 in conjunction form a ring optionally containing heteroatom(s), wherein the ring may be fused with a benzene ring optionally having substituent(s);

R^4 is alkoxycarbonyl, aminocarbonyl, hydrazinocarbonyl, alkylthiocarbonyl, formyl, carbamoyl, alkylthio, phenylthio, alkylsulfinyl, phenylsulfinyl, alkylsulfonyl, phenylsulfonyl, dialkylphosphinyl, dialkylphosphonyl, cyano or nitro; and

R^5 is hydrogen, cyano, formyl, alkyl, cycloalkyl, alkoxyalkyl, phenoxyalkyl, dialkoxyalkyl, hydroxyalkyl, haloalkyl, carboxyalkyl, cycloalkoxyalkyl, phenylthio, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, alkoxycarbonylalkyl, alkoxycarbonylethenyl, aryl optionally having substituent(s) (particularly phenyl), an aromatic heterocyclic group or phenylalkyl, or a group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3 heteroatom(s), which is fused with a benzene ring,

or R^4 and R^5 in conjunction may form a 5 or 6 membered ring optionally containing heteroatom(s),

provided that when R^0 , R^1 and R^2 are each hydrogen, R^4 is methoxycarbonyl and R^5 is methyl, then R^3 should not be phenyl, 2-chlorophenyl, 3-nitrophenyl, 4-carboxyphenyl or 4-methoxycarbonylphenyl,

5 or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

2. The dihydropyrazolopyridine compound of the above-described 1, wherein R^5 is alkyl having 2 to 8 carbon atoms, cycloalkyl, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, phenyl optionally
10 having substituent(s), an aromatic heterocyclic group or phenylalkyl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

3. The dihydropyrazolopyridine compound of the above-described 1, wherein R^1 is hydrogen, alkyl, phenyl optionally having
15 substituent(s), an aromatic heterocyclic group or phenylalkyl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

4. The dihydropyrazolopyridine compound of the above-described 1, wherein R^2 is hydrogen or alkyl, or an optically active form
20 thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

5. The dihydropyrazolopyridine compound of the above-described 1, wherein R^3 is phenyl optionally having 1 to 3 substituent(s), naphthyl, 2,1,3-benzoxadiazol-4-yl or 3,4-dihydro-2H-
25 benzopyran-8-yl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

6. The dihydropyrazolopyridine compound of the above-described 1, wherein R^4 is alkoxy carbonyl having 2 to 5 carbon atoms, cyano or nitro, or an optically active form thereof, a
30 pharmaceutically acceptable salt thereof or a hydrate thereof.

7. The dihydropyrazolopyridine compound of the above-described 1, wherein R^5 is alkyl having 2 to 4 carbon atoms, cyclopropyl, phenyl, thienyl or hydroxyalkyl, or an optically active form

thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

8. The dihydropyrazolopyridine compound of the above-described 1, wherein R² and R³ in conjunction form a ring containing
5 sulfur atom and the ring is condensed with a benzene ring optionally having substituent(s), or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

9. The dihydropyrazolopyridine compound of the above-described
10 1, wherein R⁰ is hydrogen or a group of the formula: -COOR⁸ (wherein R⁸ is alkyl, aryl optionally having substituent(s) or aralkyl optionally having substituent(s)), or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

15 10. The dihydropyrazolopyridine compound of the above-described 1, which is selected from
(32) ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(47) ethyl 4-(2-chloro-3-trifluoromethylphenyl)-4,7-dihydro-6-
20 propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(66) ethyl 4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(73) ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
25 (87) ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(116) ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(122) 4-(2,3-dichlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-
30 pyrazolo[3,4-b]pyridine,
(140) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
(147) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-phenyl-

- 2H-pyrazolo[3,4-b]pyridine,
(158) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine,
(171) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-
5 (thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine,
(182) ethyl 4-(2-bromo-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(183) ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
10 (189) 4-(2-bromo-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
(205) ethyl 2-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(240) ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-ethyl-4,7-dihydro-
15 2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(257) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-pyrazolo[3,4-b]pyridine,
(260) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine,
20 (264) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine, and
(268) 4-(2-bromo-3-cyanophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine,

a tautomer, an optically active form thereof, a
25 pharmaceutically acceptable salt thereof or a hydrate thereof.

11. A medicament comprising a dihydropyrazolopyridine compound of the above-described 1, an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

12. A pharmaceutical composition comprising a
30 dihydropyrazolopyridine compound of the above-described 1, an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof, and a pharmaceutically acceptable additive.

13. A glycogen synthase kinase-3 beta inhibitor comprising a compound selected from the group consisting of a dihydropyrazolopyridine compound of the above-described 1, an optically active form thereof, a pharmaceutically acceptable salt thereof and a hydrate thereof.
14. The medicament of the above-described 11, which is used for prevention and/or treatment of a disease caused by glycogen synthase kinase-3 beta hyperactivity.
15. The medicament of the above-described 11, which is used for prevention and/or treatment of a neurodegenerative disease.
16. The medicament of the above-described 15, wherein the disease is selected from the group consisting of Alzheimer's disease, ischemic cerebrovascular disorder, Down's syndrome, cerebral ischemia due to cerebral amyloid angiopathy, progressive supranuclear paralysis, subacute sclerosing panencephalitic Parkinsonism, postencephalitic Parkinsonism, boxer's encephalopathy, Parkinson dementia complex of Guam, Lewy body disease, Pick's disease, corticobasal degeneration, frontotemporal dementia, AIDS encephalopathy, Huntington's disease and manic-depressive psychosis.
17. The medicament of the above-described 11, which is used for prevention and/or treatment of diabetes and diabetic complications.
18. The medicament of the above-described 11, which is used as an immunopotentiator.

Brief Description of The Drawings

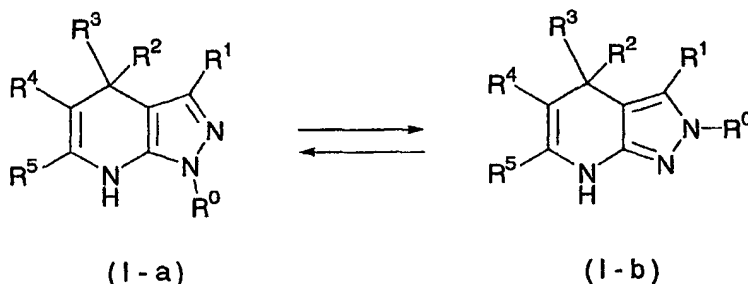
Fig. 1 shows the GSK-3 β -inhibitory activity of the compounds of Example 47 and Example 137.

Fig. 2 shows the effect of the compound of Example 66 on amyloid β -induced cytotoxicity.

Fig. 3 shows the GSK-3 β -inhibitory effect of the compound of Example 27 in a gerbil brain ischemia model.

Detailed Description of The Invention

The formula (I) indicates the presence of tautomers represented by the following formulas (I-a) and (I-b), based on the positions of hydrogen atoms of the pyrazole ring. The present invention encompasses each isomer of formulas (I-a) and (I-b), and a mixture of these isomers.



The compounds represented by the formula (I) in the present specification are described in detail in the following.

"Alkyl" means a linear or branched carbon chain of 1 to 8 carbon atom(s), and includes methyl, ethyl, propyl, butyl, pentyl(amyl), hexyl, or a structural isomer thereof, such as isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl, tert-pentyl and the like, with a preference for alkyl having 1 to 4 carbon atom(s). The alkyl of R⁵ is preferably alkyl having 2 to 8 carbon atoms. The "alkyl having 2 to 8 carbon atoms" concretely includes ethyl, propyl, butyl, pentyl(amyl), hexyl, heptyl and octyl, or a structural isomer thereof, such as isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl, tert-butyl and the like. Alkyl having 2 to 4 carbon atoms is more preferable, and propyl is particularly preferable.

"Acyl" includes alkylcarbonyl having 2 to 8 carbon atoms, such as acetyl, propionyl, butyryl, isobutyryl, valeryl, pivaloyl, hexanoyl, heptanoyl and the like, and aromatic acyl having 7 to 12 carbon atoms, such as benzoyl, naphthoyl, cinnamoyl, benzylcarbonyl and the like. The benzene and naphthalene rings may have 1 to 5 substituent(s).

"Cycloalkyl" means a cyclic carbon chain of 3 to 8 carbon atoms. Cycloalkyl concretely includes, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and the like, with a preference for cycloalkyl having 3 to 6 carbon atoms.

"Halogen" represents fluorine, chlorine, bromine or iodine.

"Amino" is primary amino, or secondary or tertiary amino having the above alkyl, and includes, for example, amino, methylamino, dimethylamino, ethylamino, diethylamino, propylamino, dipropylamino, butylamino, dibutylamino and the like, with a preference for tertiary amino containing alkyl having 1 to 4 carbon atom(s).

"Alkylthio" is a linear or branched alkylthio having 1 to 6 carbon atom(s), and includes, for example, methylthio, ethylthio, propylthio, butylthio, pentylthio(amythio), hexylthio and structural isomers thereof, such as isopropylthio, isobutylthio, sec-butylthio, tert-butylthio, isopentylthio, neopentylthio, tert-pentylthio and the like, with a preference for alkylthio having 1 to 3 carbon atom(s).

"Haloalkyl" is the above alkyl substituted by 1 to 5 halogen(s), and represents fluoromethyl, chloromethyl, difluoromethyl, trifluoromethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-pentafluoropropyl and the like.

"Aminoalkyl" is the above-mentioned alkyl having the above amino, and includes, for example, aminomethyl, methylaminomethyl, dimethylaminomethyl, 2-aminoethyl, 2-methylaminoethyl, 2-dimethylaminoethyl, 2-ethylaminoethyl, 2-diethylaminoethyl and the like, with a preference for aminoalkyl containing alkyl having 1 to 4 carbon atom(s) having tertiary amino.

"Acylamino" is acylamino having the above acyl, and represents, for example, acetylamino, propionylamino,

butyrylamino, valerylamino, pivaloylamino, benzoylamino, phenylacetyl amino, phenylpropionyl amino, phenylbutyrylamino and the like.

"Alkoxy" is alkoxy having the above alkyl, and includes, 5 for example, methoxy, ethoxy, propoxy, butoxy, pentyloxy(amyloxy), hexyloxy and structural isomers thereof, such as isopropoxy, isobutoxy, sec-butoxy, tert-butoxy, isopentyloxy, neopentyloxy, tert-pentyloxy and the like, with a preference for alkoxy having 1 to 4 carbon atom(s).

10 "Cycloalkoxy" is alkoxy having the above cycloalkyl, and includes, for example, cyclopropoxy, cyclobutoxy, cyclopentyloxy, cyclohexyloxy and the like, with a preference for cycloalkoxy having cycloalkyl having 3 to 6 carbon atoms.

"Phenylalkoxy" is phenylalkoxy having the above alkoxy, 15 and includes, for example, benzyloxy, 1-phenylethoxy, 2-phenylethoxy, 3-phenylpropoxy, 4-phenylbutoxy, 1-methyl-1-phenylethoxy, 1-methyl-2-phenylethoxy, 1-phenylpropoxy, 2-phenylpropoxy, 1-methyl-1-phenylpropoxy, 1-methyl-2-phenylpropoxy, 1-methyl-3-phenylpropoxy and the like, with a 20 preference for phenylalkoxy containing alkoxy having 1 to 4 carbon atom(s).

"Aminoalkoxy" is aminoalkoxy consisting of the above alkoxy and amino, and includes, for example, aminomethoxy, methylaminomethoxy, dimethylaminomethoxy, 2- 25 dimethylaminoethoxy, 3-dimethylaminopropoxy, 4-dimethylaminobutoxy and the like, with a preference for aminoalkoxy consisting of tertiary amino containing alkyl having 1 to 4 carbon atom(s), and alkoxy having 1 to 4 carbon atom(s).

30 "Alkoxyalkyl" is alkoxyalkyl consisting of the above alkoxy and alkyl, and includes, for example, methoxymethyl, ethoxymethyl, 2-methoxyethyl, propoxymethyl, isopropoxymethyl and the like, with a preference for alkoxyalkyl consisting of

alkoxy having 1 to 4 carbon atom(s) and alkyl having 1 to 4 carbon atom(s).

"Phenoxyalkyl" is phenoxyalkyl containing the above alkyl, and includes, for example, phenoxymethyl, 2-
5 phenoxyethyl, 3-phenoxypropyl and the like, with a preference for phenoxyalkyl containing alkyl having 1 to 4 carbon atom(s).

"Dialkoxyalkyl" is dialkoxyalkyl consisting of the above alkyl and alkoxy, and includes, for example, dimethoxymethyl, diethoxymethyl, 2,2-dimethoxyethyl, 2,2-diethoxyethyl and the
10 like, with a preference for dialkoxyalkyl consisting of alkoxy having 1 to 4 carbon atom(s) and alkyl having 1 to 4 carbon atom(s).

"Hydroxyalkyl" is hydroxyalkyl having the above alkyl, and includes, for example, hydroxymethyl, 2-hydroxyethyl, 3-
15 hydroxypropyl and the like, with a preference for hydroxylalkyl containing alkyl having 1 to 4 carbon atom(s).

"Alkoxy carbonyl" is alkoxy carbonyl having the above alkoxy, and includes, for example, methoxy carbonyl, ethoxy carbonyl, propoxy carbonyl, butoxy carbonyl,
20 pentyloxy carbonyl, hexyloxy carbonyl and structural isomers thereof, such as isopropoxy carbonyl, isobutoxy carbonyl, sec-butoxy carbonyl, tert-butoxy carbonyl, isopentyloxy carbonyl, neopentyloxy carbonyl, tert-pentyloxy carbonyl and the like, with a preference for alkoxy carbonyl, in which the alkoxy
25 moiety has 1 to 4 carbon atom(s). However, R⁴ is preferably alkoxy carbonyl having 2 to 5 carbon atoms.

"Aminocarbonyl" is aminocarbonyl having the above amino, and includes, for example, aminocarbonyl (carbamoyl), methylaminocarbonyl, dimethylaminocarbonyl, ethylaminocarbonyl,
30 diethylaminocarbonyl, propylaminocarbonyl, dipropylaminocarbonyl, phenylcarbamoyl, benzylcarbamoyl and the like, with a preference for tertiary-aminocarbonyl containing alkyl having 1 to 4 carbon atom(s).

"Alkylthiocarbonyl" is alkylthiocarbonyl having the above alkylthio, and includes, for example, methylthiocarbonyl, ethylthiocarbonyl, propylthiocarbonyl, butylthiocarbonyl and structural isomers thereof, such as isopropylthiocarbonyl, 5 isobutylthiocarbonyl, sec-butylthiocarbonyl, tert-butylthiocarbonyl and the like, with a preference for alkylthiocarbonyl, in which the alkyl moiety has 1 to 3 carbon atoms.

"Carboxyalkyl" is carboxyalkyl having the above alkyl, 10 and includes, for example, carboxymethyl, carboxyethyl, carboxypropyl and the like, with a preference for carboxyalkyl containing alkyl having 1 to 4 carbon atom(s).

"Cycloalkoxyalkyl" is cycloalkoxyalkyl having the above cycloalkoxy and alkyl, and includes, for example, 15 cyclopropoxymethyl, cyclopropoxyethyl, cyclobutoxymethyl, cyclopentyloxymethyl, cyclohexyloxymethyl and the like, with a preference for cycloalkoxyalkyl consisting of cycloalkoxy having 3 to 6 carbon atoms and alkyl having 1 to 4 carbon atom(s).

20 "Alkylsulfinyl" is alkylsulfinyl having the above alkyl, and includes, for example, methylsulfinyl, ethylsulfinyl, propylsulfinyl, isopropylsulfinyl and the like, with a preference for alkylsulfinyl containing alkyl having 1 to 4 carbon atom(s).

25 "Alkylsulfonyl" is alkylsulfonyl having the above alkyl, and includes, for example, methylsulfonyl, ethylsulfonyl, propylsulfonyl, isopropylsulfonyl and the like, with a preference for alkylsulfonyl containing alkyl having 1 to 4 carbon atom(s).

30 "Mercaptoalkyl" is mercaptoalkyl having the above alkyl, and includes, for example, mercaptomethyl, mercaptoethyl, mercaptopropyl and the like, with a preference for mercaptoalkyl containing alkyl having 1 to 4 carbon atom(s).

"Alkylthioalkyl" is alkylthioalkyl having the above alkylthio and alkyl, and includes, for example, methylthiomethyl, methylthioethyl, methylthiopropyl, ethylthiomethyl, ethylthioethyl, ethylthiopropyl and the like, with a preference for alkylthioalkyl consisting of alkylthio having 1 to 3 carbon atom(s) and alkyl having 1 to 4 carbon atom(s).

"Aryl" is aryl having 6 to 14 carbon atoms, and includes, for example, phenyl, 1-naphthyl, 2-naphthyl, 1-anthryl, 2-anthryl and the like. They may have 1 to 5 substituent(s) and substitution sites are not particularly limited.

"Aralkyl" is aralkyl wherein the above alkyl is substituted by the above aryl, and includes benzyl, 2-phenylethyl, 3-phenylpropyl, 1-naphthylmethyl, 2-naphthylmethyl and the like. These may have 1 to 5 substituent(s) on the aryl moiety.

"Acyloxyacetyl" is acyloxyacetyl having the above acyl, and includes, for example, acetyloxyacetyl, propionyloxyacetyl, butyryloxyacetyl, benzoyloxyacetyl and the like.

"Acyloxyalkyl" is acyloxyalkyl having the above acyl and alkyl, and includes, for example, acetyloxymethyl, propionyloxymethyl, butyryloxymethyl, benzoyloxymethyl, 2-acetyloxyethyl, 2-propionyloxyethyl, 2-butyryloxyethyl, 2-benzoyloxyethyl and the like.

The substituent of the "phenyl optionally having substituent(s)" is exemplified by those mentioned for the "substituent" below, wherein the number of the substituent is generally 1 to 5, preferably 3. Phenyl having 1 or 2 substituent(s) is particularly preferable.

"Aromatic heterocyclic group" is a 5- or 6-membered aromatic heterocyclic ring optionally containing 1 to 3 heteroatom(s) of nitrogen atom, oxygen atom and sulfur atom, and includes, for example, thiophene, furan, pyrrole,

imidazole, pyrazole, thiazole, isothiazole, oxazole, isoxazole, pyridine, pyridazine, pyrimidine, pyrazine and the like.

The substituent of the "aromatic heterocyclic ring optionally having substituent(s)" is exemplified by those
5 mentioned for the "substituent" below, wherein the number of the substituent is generally 1 to 5, preferably 3.

"Phenylalkyl" is phenylalkyl having the above alkyl, and includes, for example, benzyl, 2-phenylethyl, 3-phenylpropyl, 4-phenylbutyl, 1-phenylethyl, 1-methyl-2-phenylethyl, 1-
10 phenylpropyl, 2-phenylpropyl, 1-methyl-1-phenylpropyl, 1-methyl-2-phenylpropyl, 1-methyl-3-phenylpropyl and the like, with a preference for phenylalkyl consisting of phenyl and alkyl having 1 to 4 carbon atom(s).

The kind and the number of the substituent of the
15 "phenylalkyl optionally having substituent(s)" are the same as those for the above-mentioned "aromatic heterocyclic ring".

"Alkoxy carbonylalkyl" is alkoxy carbonylalkyl having the above alkoxy carbonyl and alkyl, and includes, for example, methoxycarbonylmethyl, ethoxycarbonylmethyl,
20 ethoxycarbonylmethyl, 2-ethoxycarbonylethyl, 3-ethoxycarbonylpropyl and the like.

"Alkoxy carbonylethenyl" is alkoxy carbonylethenyl having the above alkoxy carbonyl, and includes, for example, 2-methoxycarbonylethenyl, 2-ethoxycarbonylethenyl, 2-
25 butoxycarbonylethenyl, 2-tert-butoxycarbonylethenyl and the like.

"Dialkylphosphinyl" is dialkylphosphinyl having the above alkyl, and includes, for example, dimethylphosphinyl, diethylphosphinyl, dipropylphosphinyl and the like, with a
30 preference for dialkylphosphinyl containing alkyl having 1 to 4 carbon atom(s).

"Dialkylphosphonyl" is dialkylphosphonyl having the above alkyl, and includes, for example, dimethylphosphonyl,

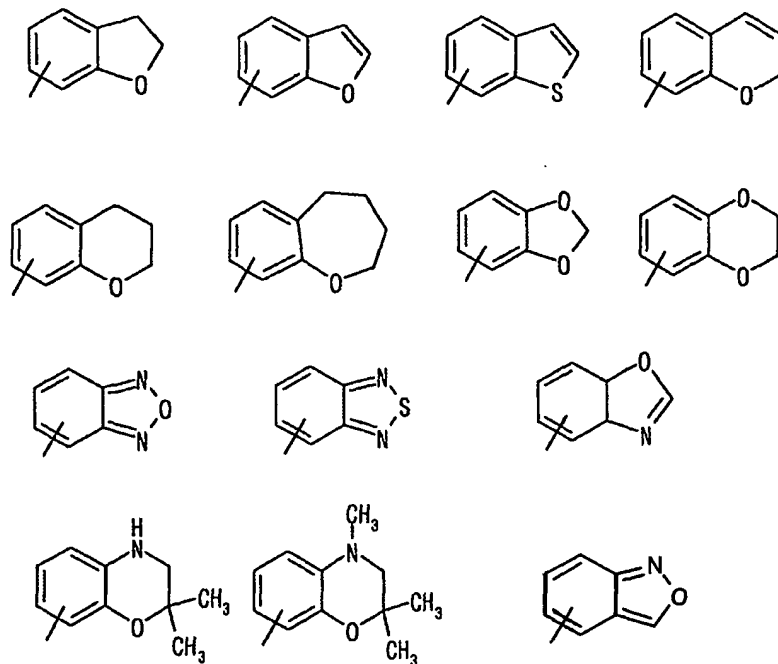
diethylphosphonyl, dipropylphosphonyl and the like, with a preference for dialkylphosphonyl containing alkyl having 1 to 4 carbon atom(s).

In the present specification, "substituent" includes
5 alkyl, acyl, cycloalkyl, phenyl, aromatic heterocyclic ring, phenylalkyl, hydroxy, thiol, halogen, amino, formyl, carbamoyl, cyano, nitro, alkylthio, haloalkyl, aminoalkyl, acylamino, alkoxy, cycloalkoxy, phenoxy, phenylalkoxy, aminoalkoxy, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, alkoxycarbonyl,
10 alkylsulfinyl, aminocarbonyl, alkylthiocarbonyl and the like.

"Ring optionally containing heteroatom(s)" is a 5 or 6 membered carbocyclic ring optionally containing 1 to 3 heteroatom(s) consisting of nitrogen atom, oxygen atom and sulfur atom, with particular preference given to a ring
15 containing sulfur atom. The ring may be substituted by one or more of the above substituents or oxo groups. The substitution site is not particularly limited. This ring is formed by R^2 and R^3 in the formula (I) together with the attached carbon atom. By forming this ring, a spiro ring is formed in the
20 compound of the formula (I). The above ring can be fused with a benzene ring optionally having substituent(s). Such a ring includes, for example, 2,3-dihydrobenzo[b]thiophene, 2,3-dihydrobenzo[b]thiophen-1-oxide and the like.

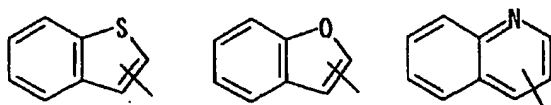
"A group derived from a benzene ring, which is fused
25 with a saturated or unsaturated 5 or 6 membered carbocyclic ring" represents a group derived from naphthalene, 1,2-dihydronaphthalene, 1,2,3,4-tetrahydronaphthalene, indan and the like, with preference given to naphthalene (namely naphthyl) and particular preference given to 1-naphthyl.

30 "A group derived from a benzene ring fused with a saturated or unsaturated 5 to 7 membered carbocyclic ring containing 1 to 3 heteroatom(s)" includes the following groups and the like.



Of these, 2,1,3-benzoxadiazole and 3,4-dihydro-2H-benzopyrane are preferable, and 2,1,3-benzoxadiazol-4-yl and 3,4-dihydro-2H-benzopyran-8-yl are particularly preferable.

5 "A group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3 heteroatom(s), which is fused with a benzene ring" includes the following groups and the like.

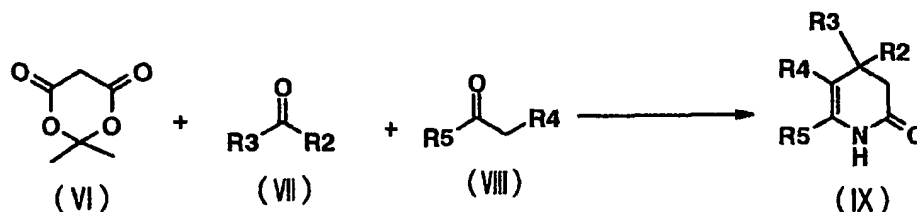


10 The "5 or 6-membered ring optionally containing heteroatom(s)" is a 5 or 6 membered carbocyclic ring optionally containing 1 to 3 heteroatom(s) consisting of nitrogen atom, oxygen atom and sulfur atom. Examples thereof include furan, thiophene, pyrrole, oxazole, isoxazole,
 15 thiazole, isothiazole, imidazole, pyrazole, furazan, pyran, pyridine, pyridazine, pyrimidine, pyrazine, pyrroline, pyrrolidine, imidazoline and imidazolidine. Of these, furan,

thiophene, pyrrole, oxazole, isoxazole, thiazole, isothiazole, furazan and pyridine are preferable.

The compounds, represented by the formula (I) of the present invention can be converted to acid addition salts with
 5 pharmaceutically acceptable acids and such acid addition salts are also encompassed in the present invention. Such acid addition salts include, for example, salts with inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, nitric acid, phosphoric acid and the like,
 10 and salts with organic acids such as formic acid, acetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, citric acid, tartaric acid, methanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, glutamic acid and the like.
 15 Furthermore, the compounds of the present invention can form hydrates, solvates with ethanol and the like, and crystal polymorphs. When an asymmetric carbon atom exists, optical isomers and racemates thereof can be present, and all of these are encompassed in the present invention.

20 Of the compounds (I) of the present invention, a compound wherein R⁰ is hydrogen can be synthesized as shown in the following according to the method described in J. Chem. Soc., Perkin Trans. 1, 947 (1996) and the like.
 (First Production Method)

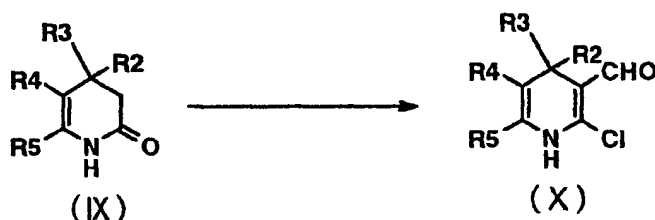


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wherein R², R³, R⁴ and R⁵ are as defined above.

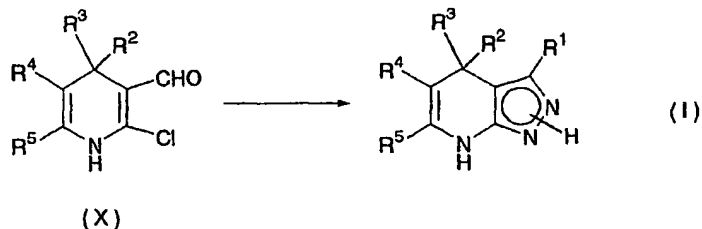
Meldrum's acid of the formula (VI) and a carbonyl derivative of the formula (VII) are reacted with a carbonyl

derivative of the formula (VIII) to give an amide derivative of the formula (IX). The reaction is carried out in the presence of a carboxylic acid solvent inert to the reaction. As the solvent, formic acid, acetic acid, propionic acid, butyric acid, valeric acid and the like are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.



wherein R², R³, R⁴ and R⁵ are as defined above.

The obtained amide derivative of the formula (IX) is reacted in the presence of dimethylformamide and phosphorus oxychloride to give a formyl derivative of the formula (X). The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, ether, tetrahydrofuran, dioxane, ethyl acetate, acetonitrile, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethyl sulfoxide and the like are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.

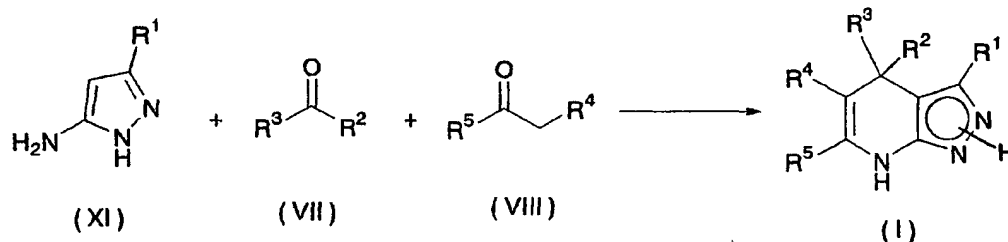


wherein R¹ represents hydrogen, and R², R³, R⁴ and R⁵ are as defined above.

The compound (I) of the present invention can be produced by reacting the obtained formyl derivative of the

formula (X) in the presence of hydrazine. The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, ether, tetrahydrofuran, dioxane, ethyl acetate, acetonitrile, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethyl sulfoxide, pyridine, alcohol and the like are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.

The carbonyl derivative of the formula (VII), which is a starting material, can be synthesized according to the methods described in J. Org. Chem., 46, 783 (1981), Eur. J. Med. Chem., 31, 3 (1996) and Tetrahedron Lett., 24, 5023 (1983). The carbonyl derivative of the formula (VIII) can be synthesized according to the method described in Synthesis, 290 (1993). (Second Production Method)

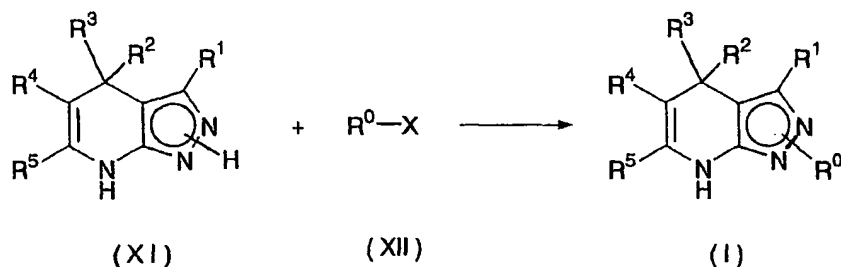


wherein R¹, R², R³, R⁴ and R⁵ are as defined above.

The compounds (I) of the present invention can be produced by reacting aminopyrazole of the formula (XI) and a carbonyl derivative of the formula (VII) with a carbonyl derivative of the formula (VIII). The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, ether, tetrahydrofuran, dioxane, ethyl acetate, acetonitrile, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethyl sulfoxide, alcohol and the like are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.

Of the compounds (I) of the present invention, a compound wherein R^0 is a substituent other than hydrogen can be synthesized as follows.

(Third Production Method)



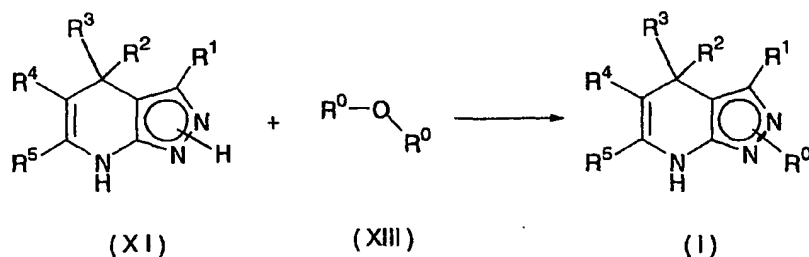
5

wherein R^0 , R^1 , R^2 , R^3 , R^4 and R^5 are as defined above, and X represents halogen, provided that R^0 is not hydrogen.

The compounds (I) of the present invention can be produced by reacting a dihydropyrazolopyridine derivative of the formula (XI) with halide of the formula (XII) in the presence of a base. Suitable base includes, for example, triethylamine, diisopropylethylamine, 4-dimethylaminopyridine and the like. The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, one without

15 hydroxy group is generally used, such as tetrahydrofuran, ethyl acetate, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethylimidazolidinone and the like. The reaction is carried out at any temperature, for example, from -10°C to 200°C , preferably from 0°C to 100°C .

20 (Fourth Production Method)



wherein R^0 , R^1 , R^2 , R^3 , R^4 and R^5 are as defined above, provided

that R⁰ is not hydrogen.

The compounds (I) of the present invention can be produced by reacting a dihydropyrazolopyridine derivative of the formula (XI) with anhydride of the formula (XIII) in the presence of a base. Suitable base includes, for example, triethylamine, pyridine, 4-dimethylaminopyridine and the like. The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, one without hydroxy group is generally used, such as tetrahydrofuran, ethyl acetate, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethylimidazolidinone, pyridine and the like. The reaction is carried out at any temperature, for example, from -10°C to 200°C, preferably from 0°C to 100°C.

The compound (I) of the present invention thus produced can be isolated and purified as a free compound or a salt thereof. Isolation and purification is carried out by a conventional chemical process such as extraction, concentration, evaporation, crystallization, filtration, recrystallization, various kinds of chromatography and the like. When the purified product obtained is a racemate, a desired optically active compound can be separated by, for example, fractional recrystallization with optically active acid, or passing through a column packed with optically active carrier. The present invention also encompasses optically active compounds.

The compounds of the present invention obtained by the above methods have a weak inhibitory activity on kinases other than GSK-3 β such as CaM kinase II, MAP kinase, Casein kinase, PKA, PKC and ROCK, but have a strong inhibitory activity on GSK-3 β . Therefore, the compounds of the present invention have a GSK-3 β -selective inhibitory activity and can be medicaments with small side-effect for diabetes, diabetic complications and neurodegenerative diseases (Alzheimer's disease, ischemic

cerebrovascular disorders, Down's syndrome, cerebral ischemia due to cerebral amyloid angiopathy, progressive supranuclear paralysis, subacute sclerosing panencephalitic Parkinsonism, postencephalitic Parkinsonism, boxer's encephalopathy, 5 Parkinsonism dementia complex of Guam, Lewy body disease, Pick's disease, corticobasal degeneration, frontotemporal dementia, AIDS encephalopathy, Huntington's disease, manic-depressive psychosis and the like). In addition, the compounds of the present invention are useful as immunopotentiators.

10 Formulations comprising the compounds of the present invention or salts thereof as an active ingredient are prepared using carriers, excipients and other additives conventionally used for formulation. The carrier and excipient for formulation may be a solid or liquid, and 15 include, for example, lactose, magnesium stearate, starch, talc, gelatin, agar, pectin, gum Arabic, olive oil, sesame oil, cacao butter, ethylene glycol and other conventionally used substances. Administration may be oral administration of tablet, pill, capsule, granule, powder, solution and the like, 20 or parenteral administration of injection (intravenous injection, intramuscular injection and the like), suppository, transdermal agent and the like. While the dose is appropriately determined on each case in consideration of symptom, age and sex of the administration subject, and the 25 like, it is generally 1 - 1,000 mg, preferably 50 - 200 mg per day for an adult person, which is orally administered once to several times a day, or 1 - 500 mg per day for an adult person, which is intravenously administered once to several times a day, or continuously administered intravenously for 1 to 24 30 hours a day.

As solid compositions for oral administration according to the present invention, tablet, powder, granule and the like are used. In such a solid composition, one or more active

substances are mixed with at least one inert diluent, such as lactose, mannitol, glucose, hydroxypropylcellulose, microcrystalline cellulose, starch, polyvinylpyrrolidone, metasilicic acid and magnesium aluminate. The composition may
5 contain, according to a conventional method, inert additives other than diluent, for example, a lubricant such as magnesium stearate, a disintegrator such as cellulose and calcium glycolate, a stabilizer such as lactose and a solubilizer such as glutamic acid and aspartic acid. Tablet and pill may be
10 coated with a gastric or enteric coating film of, for example, sucrose, gelatin, hydroxypropylcellulose and the like. Liquid compositions for oral administration include pharmaceutically acceptable emulsion, solution, suspension, syrup, elixir and the like, and contain an inert diluent generally used, such as
15 purified water and ethanol. This composition may contain an adjuvant such as wetting agent and suspending agent, a sweetener, a flavor, an aromatic and an antiseptic, in addition to the inert diluent. Injections for parenteral administration contain sterile aqueous or non-aqueous solution,
20 suspension and emulsion. The aqueous solution and suspension include, for example, propylene glycol, polyethylene glycol, vegetable oil such as olive oil, alcohols such as ethanol, polysorbate 80 and the like. Such a composition may contain adjuvants such as antiseptic, wetting agent, emulsifier,
25 dispersant, stabilizer and solubilizer. These are sterilized by, for example, filtration through a bacteria-retaining filter, addition of an antimicrobial agent, irradiation of ultraviolet ray and the like. Alternatively, a sterile solid composition may be prepared and used upon dissolution in
30 sterile water or sterile solvent for injection prior to use.

Examples

The present invention is described in detail in the following, based on Examples, Formulation Examples and

Experimental Examples. The scope of the present invention is not limited to these examples.

Example 1

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-
5 b]pyridine-5-carboxylate

A solution of 2-chlorobenzaldehyde (1.7 g), 3-aminopyrazole (1.0 g) and ethyl acetoacetate (1.6 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature and the
10 solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane- ethyl acetate (8:2)) to give the title compound (850 mg) as colorless crystals.

Melting Point (MP): 217-221°C.

15 Anal. Calcd. for: $C_{16}H_{16}N_3O_2Cl$: C, 60.47; H, 5.08; N, 13.22.

Found: C, 60.15; H, 5.07; N, 13.53.

MS (EI): 317 (M⁺).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.00 (3H, t, J=6.8Hz), 2.25 (3H, s),
3.72-3.82 (2H, m), 5.57 (1H, s), 7.07-7.12 (2H, m),
20 7.18 (1H, d, J=7.3Hz), 7.26 (1H, s), 7.34 (1H, d, J=7.9Hz),
9.53 (1H, br. s), 11.98 (1H, br. s).

IR (KBr): ν =3393, 3267, 1670, 1589, 1518, 1278, 1217 cm^{-1} .

Example 2

Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-methyl-2H-
25 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl acetoacetate in the same manner as in Example 1.

MP: 196-200°C.

30 Anal. Calcd. for: $C_{17}H_{19}N_3O \cdot 1/5 H_2O$: C, 64.42; H, 6.17; N, 13.26.

Found: C, 64.08; H, 6.05; N, 13.68.

MS (EI): 313 (M⁺).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.00 (3H, t, J=6.8Hz), 2.81 (3H, s),

3.72 (3H, s), 3.87 (2H, q, J=6.8 Hz), 5.54 (1H, s), 6.80 (1H, dd, J=7.3 Hz and 7.4 Hz), 6.90 (1H, d, J=7.8 Hz), 7.04 (1H, d, J=7.4 Hz), 7.13-7.15 (2H, m), 9.99 (1H, br. s), 11.98 (1H, br. s).

IR (KBr): ν =3362, 3267, 3204, 3090, 1662, 1589, 1516, 1275, 1097 cm^{-1} .

5 Example 3

Ethyl 4,7-dihydro-6-methyl-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl acetoacetate in the same manner as in Example 1.

MP: 259-262°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{16}\text{F}_3\text{N}_3\text{O}_2 \cdot 1/5 \text{H}_2\text{O}$: C, 57.53; H, 4.66; N, 11.84.

Found: C, 57.56; H, 4.68; N, 11.86.

MS (EI): 352 ($\text{M}^+ + 1$).

15 ^1H -NMR (400 MHz, DMSO- d_6) δ (ppm): 0.74 (3H, t, J=6.9 Hz), 2.40 (3H, s), 3.68-3.81 (2H, m), 5.42 (1H, s), 7.00 (1H, s), 7.28 (1H, dd, J=7.3 Hz and 7.4 Hz), 7.33 (1H, d, J=7.2 Hz), 7.51 (1H, dd, J=7.3 Hz and 7.4 Hz), 7.60 (1H, d, J=7.8 Hz), 9.58 (1H, br. s), 12.00 (1H, br. s).

IR (KBr): ν =3277, 3209, 3094, 1668, 1593, 1514, 1313, 1213, 1153, 1097, 20 765 cm^{-1} .

Example 4

Methyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and methyl acetoacetate in the same manner as in Example 1.

MP: 235°C.

Anal. Calcd. for: $\text{C}_{15}\text{H}_{14}\text{ClN}_3\text{O}_2 \cdot 2/5 \text{H}_2\text{O}$: C, 57.94; H, 4.80; N, 13.51.

Found: C, 58.03; H, 4.55; N, 13.43.

30 MS (EI): 303 (M^+).

^1H -NMR (400 MHz, DMSO- d_6) δ (ppm): 2.40 (3H, s), 3.34 (3H, s), 5.55 (1H, s), 7.09-7.11 (2H, m), 7.18 (1H, dd, J=7.3 Hz and 7.4 Hz), 7.29 (1H, s), 7.34 (1H, d, J=7.3 Hz), 9.57 (1H, br. s), 12.00 (1H, br. s).

Example 5

t-Butyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and t-butyl acetoacetate in the same manner as in Example 1.

MP:207°C.

Anal. Calcd. for: C₁₈H₂₀ClN₃O₂: C, 62.52; H, 5.83; N, 12.15.

Found: C, 62.51; H, 5.79; N, 12.17.

10 MS(EI): 345(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.07(9H, s), 2.36(3H, s), 5.50(1H, s), 7.11-7.15(2H, m), 7.20(1H, d, J=7.3Hz), 7.25(1H, s), 7.37(1H, d, J=7.3Hz), 9.35(1H, br.s), 11.93(1H, br.s).

Example 6

15 Isopropyl 4-(2-fluorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and isopropyl acetoacetate in the same manner as in Example 1.

20 MP:218-220°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.66(3H, d, J=6.3Hz), 1.02(3H, d, J=6.3Hz), 2.37(3H, s), 4.66(1H, q, J=6.3Hz), 5.40(1H, s), 7.01-7.14(4H, m), 7.19(1H, s), 9.46(1H, br.s), 11.97(1H, br.s).

Example 7

25 Benzyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and benzyl acetoacetate in the same manner as in Example 1.

30 MP:234°C.

Anal. Calcd. for: C₂₁H₁₈ClN₃O₂: C, 66.40; H, 4.78; N, 11.06.

Found: C, 66.16; H, 4.86; N, 10.92.

MS(EI): 379(M⁺).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 2.43(3H, s), 4.81(1H, d, $J=12.6\text{Hz}$), 4.92(1H, d, $J=12.6\text{Hz}$), 5.62(1H, s), 6.86-6.88(2H, m), 7.13-7.18(6H, m), 7.31-7.34(2H, m), 9.65(1H, br. s), 12.01(1H, br. s).

Example 8

5 4-(2-Chlorophenyl)-5-dimethylaminocarbonyl-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and N,N-dimethylacetamide in the same manner as in Example 1.

10 MP: 229°C.

Anal. Calcd. for: $\text{C}_{16}\text{H}_{17}\text{ClN}_4\text{O} \cdot 1/2 \text{H}_2\text{O}$: C, 58.99; H, 5.57; N, 17.20.

Found: C, 58.90; H, 5.46; N, 16.84.

MS(EI): 316(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.77(3H, s), 2.72(6H, s),
15 5.39(1H, s), 7.10-7.22(4H, m), 7.30(1H, d, $J=7.3\text{Hz}$), 8.40(1H, br. s), 11.83(1H, br. s).

Example 9

4-(2-Chlorophenyl)-5-hydrazinocarbonyl-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine

20 To a solution of 4-(2-chlorophenyl)-4,7-dihydro-5-dimethylaminocarbonyl-6-methyl-2H-pyrazolo[3,4-b]pyridine (200 mg) in acetonitrile (200 mL) was added hydrazine (200 mg) and the mixture was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated
25 crystals were collected by filtration and washed with ethyl acetate to give the title compound as colorless crystals (150 mg).

MP: 220°C.

Anal. Calcd. for: $\text{C}_{14}\text{H}_{14}\text{ClN}_5\text{O} \cdot 3/10 \text{H}_2\text{O}$: C, 54.39; H, 4.76; N, 22.65.

30 Found: C, 54.36; H, 4.56; N, 22.65.

MS(EI): 303(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.85(3H, s), 3.20-3.80(3H, br. s), 5.15(1H, s), 6.81(1H, s), 7.16-7.028(3H, m), 7.34(1H, d, $J=7.3\text{Hz}$),

10.05-11.07 (2H, brs).

Example 10

4-(2-Fluorophenyl)-4,7-dihydro-6-methyl-5-isopropylthiocarbonyl-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and acetoacetic acid isopropyl thioester in the same manner as in Example 1.

MP:192-194°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.03(3H, d, J=6.9Hz),
10 1.15(3H, d, J=6.9Hz), 2.43(3H, s), 3.35(1H, q, J=6.9Hz), 5.55(1H, s),
7.04-7.15(4H, m), 7.33(1H, s), 9.81(1H, br.s), 12.11(1H, br.s).

Example 11

4,7-Dihydro-6-methyl-5-nitro-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and 1-nitropropan-2-one in the same manner as in Example 1.

MP:257-258°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.65(3H, s), 5.75(1H, s),
20 7.19(1H, s), 7.30-7.35(2H, m), 7.51(1H, dd, J=7.3Hz and 7.8Hz),
7.66(1H, d, J=7.8Hz), 10.87(1H, br.s), 12.45(1H, br.s).

Example 12

Ethyl 4,7-dihydro-4-phenyl-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

25 The title compound was prepared from benzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:110-115°C.

Anal. Calcd. for: C₁₆H₁₄N₃O₂F₃ 1/2 H₂O: C, 55.49; H, 4.37; N, 12.13.

30 Found: C, 55.84; H, 4.70; N, 11.89.

MS(EI): 337(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=6.9Hz),
3.90(2H, q, J=6.8Hz), 5.54(1H, s), 7.13-7.17(3H, m), 7.24-

7.28(3H,m), 9.78(1H,br.s), 12.20(1H,br.s).

IR(KBr): ν =3375,3175,3067,1707,1606,1533,1278,1206,1197,1167 cm^{-1} .

Example 13

Ethyl 4-(2-fluorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:119-120°C.

Anal. Calcd. for: $\text{C}_{16}\text{H}_{13}\text{F}_4\text{N}_3\text{O}_2$: C, 54.09; H, 3.69; N, 11.84.

Found: C, 53.84; H, 3.57; N, 11.79.

MS(EI): 356(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.94 (3H,t, $J=6.8\text{Hz}$), 3.89(2H,q, $J=6.8\text{Hz}$), 5.46(1H,s), 7.11-7.20(4H,m), 7.28-

7.30(1H,m), 9.92(1H,br.s), 12.27(1H,br.s).

IR(KBr): ν =3290,3178,3069,1703,1608,1537,1280,1232,1174,1138, 756 cm^{-1} .

Example 14

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:171-172°C.

MS(EI): 371(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.91 (3H,t, $J=7.3\text{Hz}$), 3.50(3H,br.s), 3.87 (2H,q, $J=6.8\text{Hz}$), 5.66(1H,s), 6.26(2H,s), 7.15-7.18(2H,m), 7.27(1H,d, $J=7.8\text{Hz}$), 7.30(1H,s), 7.40(1H,d, $J=7.8\text{Hz}$), 9.65(1H,br.s).

IR(KBr): ν =3297,2935,1730,1624,1550,1479,1186 cm^{-1} .

Example 15

Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:144-146°C.

5 Anal. Calcd. for: $C_{17}H_{16}F_3N_3O_3$: C, 55.59; H, 4.39; N, 11.44.

Found: C, 55.55; H, 4.38; N, 11.43.

MS(EI): 367(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94(3H, t, J=6.8Hz), 3.83(3H, s),
3.89(2H, q, J=6.8Hz), 5.51(1H, s), 6.84(1H, dd, J=7.3Hz and 7.4Hz),
10 6.94-6.97(2H, m), 7.13(1H, dd, J=7.3Hz and 7.4Hz), 7.20(1H, s),
9.70(1H, br.s), 12.13(1H, br.s).

IR(KBr): ν =3431, 3173, 3067, 2993, 2924, 1689, 1610, 1527, 1286, 1226,
1145 cm^{-1} .

Example 16

15 Ethyl 4,7-dihydro-6-trifluoromethyl-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:182-186°C.

Anal. Calcd. for: $C_{17}H_{13}N_3O_2F_6$: C, 50.38; H, 3.23; N, 10.37.

Found: C, 50.21; H, 3.15; N, 10.39.

MS(FAB): 406($M^+ + 1$).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.83 (3H, t, J=6.8Hz),
3.83(2H, q, J=6.8Hz), 5.49(1H, s), 7.08(1H, s), 7.35-7.39(2H, m),
7.62(1H, dd, J=7.3Hz and 7.4Hz), 7.66(1H, d, J=7.8Hz),
9.97(1H, br.s), 12.30(1H, br.s).

IR(KBr): ν =3339, 3177, 3067, 1711, 1608, 1537, 1313, 1280, 1182, 1141 cm^{-1} .

30 Example 17

Ethyl 4-(3-chlorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3-

chlorobenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:144-145°C.

Anal. Calcd. for: C₁₆H₁₃N₃O₂F₃Cl: C, 51.69; H, 3.52; N, 11.30.

5 Found: C, 51.33; H, 3.74; N, 11.10.

MS(EI): 371(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.98 (3H, t, J=6.8Hz),
3.92(2H, q, J=6.8Hz), 5.21(1H, s), 7.11(1H, d, J=7.8Hz), 7.17(1H, s),
7.23(1H, d, J=8.7Hz), 7.29-7.33(2H, m), 9.92(1H, br. s),

10 12.30(1H, br. s).

IR(KBr): ν=3321, 3178, 3070, 1703, 1610, 1535, 1278, 1224, 1184, 1145cm⁻¹.

Example 18

Ethyl 4-(4-chlorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from 4-chlorobenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:176-178°C.

Anal. Calcd. for: C₁₆H₁₃F₃N₃O₂Cl: C, 51.69; H, 3.52; N, 11.30.

20 Found: C, 51.91; H, 3.77; N, 11.08.

MS(EI): 371(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.98 (3H, t, J=6.8Hz),
3.90(2H, q, J=7.3Hz), 5.92(1H, s), 7.16(2H, d, J=8.2Hz), 7.27(1H, s),
7.31(2H, d, J=8.2Hz), 9.87(1H, br. s), 12.27(1H, br. s).

25 IR(KBr): ν=3476, 3368, 3178, 3078, 1714, 1695, 1606, 1537, 1278, 1172, 1134cm⁻¹.

Example 19

Ethyl 4,7-dihydro-4-(4-methoxyphenyl)-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 4-methoxybenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:159-161°C.

Anal. Calcd. for: $C_{17}H_{16}FN_3O_3$: C, 55.59; H, 4.39; N, 11.44.

Found: C, 55.49; H, 4.54; N, 11.33.

MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.99 (3H, t, J=7.3Hz), 3.68 (3H, s),
5 3.89 (2H, q, J=7.3Hz), 5.12 (1H, s), 6.82 (2H, d, J=8.7Hz),
7.03 (2H, d, J=8.7Hz), 7.22-7.24 (1H, m), 9.71 (1H, br.s),
12.19 (1H, br.s).

IR(KBr): ν =3323, 3231, 3173, 3067, 1699, 1610, 1535, 1510, 1302, 1248, 1184, 1145 cm^{-1} .

10 Example 20

Ethyl 4-(4-ethoxycarbonylphenyl)-4,7-dihydro-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 4-ethoxycarbonylbenzaldehyde, 3-aminopyrazole and ethyl
15 trifluoroacetoacetate in the same manner as in Example 1.

MP: 157-160°C.

Anal. Calcd. for: $C_{19}H_{18}F_3N_3O_4$: C, 55.75; H, 4.43; N, 10.26.

Found: C, 55.68; H, 4.39; N, 10.43.

MS(FAB): 410 ($M^+ + 1$).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.96 (3H, t, J=6.9Hz), 1.28 (3H, t, J=7.3Hz), 3.89 (2H, q, J=6.8Hz), 4.27 (2H, q, J=7.3Hz),
5.28 (1H, s), 7.27 (1H, s), 7.29 (2H, d, J=8.3Hz), 7.87 (2H, d, J=8.2Hz),
9.92 (1H, br.s), 12.28 (1H, br.s).

IR(KBr): ν =3393, 3188, 3082, 1692, 1612, 1539, 1284 cm^{-1} .

25 Example 21

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-3-methyl-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-amino-5-methylpyrazole and ethyl
30 trifluoroacetoacetate in the same manner as in Example 1.

MP: 165-168°C.

MS(EI): 385 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94 (3H, t, J=7.3Hz), 1.81 (3H, s),

3.85(2H,q,J=6.8Hz), 5.54(1H,s), 7.17-7.20(2H,m),
7.27(1H,dd,J=7.3Hz and 7.4Hz), 7.36(1H,d,J=8.3Hz),
9.79(1H,br.s), 11.96(1H,br.s).
IR(KBr): ν =3263,3194,3080,1668,1591,1520,1286,1232,1149,1095,
5 1062cm⁻¹.

Example 22

Ethyl 4,7-dihydro-4-(thiophen-2-yl)-6-trifluoromethyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from thiophene-2-
10 aldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in
the same manner as in Example 1.

MP:157-161°C.

Anal. Calcd. for:C₁₄H₁₂F₃N₃O₂S:C,49.27;H,2.95;N,12.31.

Found:C,49.10;H,3.28;N,12.13.

15 MS(EI):343(M⁺).

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 1.08 (3H,t,J=7.4Hz), 4.00
(2H,q,J=7.4Hz), 5.52(1H,s), 6.76(1H,d,J=2.9Hz),
6.87(1H,dd,J=2.9Hz and 5.4Hz), 7.30(1H,d,J=5.4Hz), 7.43(1H,s),
9.96(1H,br.s), 12.35(1H,br.s).

20 IR(KBr): ν =3350,3240,3180,1693,1612,1535,1396,1371,1304,1153,109
3,1057,694cm⁻¹.

Example 23

Ethyl 4,7-dihydro-4-(thiophen-3-yl)-6-trifluoromethyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

25 The title compound was prepared from thiophene-3-
aldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in
the same manner as in Example 1.

MP:140-145°C.

Anal. Calcd. for:C₁₄H₁₂F₃N₃O₂S:C,49.27;H,2.95;N,12.31.

30 Found:C,49.65;H,2.64;N,12.19.

MS(EI):343(M⁺).

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 1.03 (3H,t,J=7.3Hz), 3.96
(2H,q,J=7.3Hz), 5.30(1H,s), 6.87(1H,d,J=4.8Hz), 7.05(1H,s),

7.35(1H,s), 7.39(1H,dd,J=2.9Hz and 4.8Hz), 9.76(1H,br.s),
12.25(1H,br.s).

IR(KBr): ν =3356,3182,2982,2932,1689,1614,1537,1304,1224,1153 cm^{-1} .

Example 24

5 Ethyl 4,7-dihydro-4-(1-naphthyl)-6-trifluoromethyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from naphthalene-1-aldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

10 MP:119-120°C.

Anal. Calcd. for: $\text{C}_{20}\text{H}_{16}\text{F}_3\text{N}_3\text{O}_2 \cdot 1/2 \text{H}_2\text{O}$: C, 60.45; H, 4.57; N, 10.57.

Found: C, 60.20; H, 4.77; N, 10.39.

MS(FAB): 388($\text{M}^+ + 1$).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.69 (3H,t,J=6.8Hz),
15 3.73(2H,q,J=6.8Hz), 6.04(1H,s), 7.09(1H,s), 7.26(1H,d,J=6.8Hz),
7.41(1H,dd,J=7.3Hz and 7.4Hz), 7.52-7.58(2H,m),
7.75(1H,d,J=8.3Hz), 7.92(1H,dd,J=7.3Hz and 7.4Hz), 8.33(1H,s),
9.87(1H,br.s), 12.14(1H,br.s).

IR(KBr): ν =3173,1670,1606,1138,1095 cm^{-1} .

20 Example 25

Ethyl 4,7-dihydro-4-phenyl-6-propyl-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate maleate

A solution of benzaldehyde (1.6 g), 3-aminopyrazole (1.0 g) and ethyl 3-ketohexanoate (1.9 g) in acetonitrile (20 mL)
25 was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (720 mg) as colorless
30 crystals.

MP:139-141°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{21}\text{N}_3\text{O}_2\text{C}_4\text{H}_4\text{O}_4 \cdot 1/2 \text{H}_2\text{O}$: C, 60.54; H, 6.00; N, 9.63.

Found: C, 60.16; H, 5.60; N, 10.01.

MS(EI):311(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.94-0.95 (6H,m), 1.62
(2H,q,J=7.8Hz), 2.66-2.77(2H,m), 3.50(3H,br.s),
3.83(2H,q,J=6.8Hz), 5.10(1H,s), 6.25(2H,s), 7.05-7.20(6H,m),
5 9.37(1H,br.s).

IR(KBr): ν =3337,3042,1699,1593,1467,1539,1361,1203 cm^{-1}

Example 26

Ethyl 4-(2-fluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

10 The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:192-194°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{20}\text{FN}_3\text{O}_2$ 1/2 H_2O :C,63.89;H,6.26;N,12.42.

15 Found:C,63.85;H,6.01;N,12.36.

MS(EI):329(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.93 (3H,t,J=7.3Hz), 0.97
(3H,t,J=7.3Hz), 1.62-1.68(2H,m), 2.71-2.83(2H,m),
3.82(2H,q,J=7.3Hz), 5.43(1H,s), 7.05-7.11(4H,m), 7.21(1H,s),
20 9.48(1H,br.s), 11.97(1H,br.s).

IR(KBr): ν =3265,3198,2964,1591,1514,1224,1209,1093 cm^{-1} .

Example 27

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

25 The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:202-205°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{20}\text{ClN}_3\text{O}_2$:C,62.52;H,5.83;N,12.15.

30 Found:C,62.28;H,5.76;N,12.37.

MS(FAB):346(M^++1).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.85 (3H,t,J=6.8Hz), 0.95
(3H,t,J=7.3Hz), 1.62-1.68(2H,m), 2.67-2.87(2H,m),

3.78(2H,q,J=6.8Hz), 5.58(1H,s), 7.07-7.11(2H,m),
7.18(1H,dd,J=7.3Hz and 7.4Hz), 7.25(1H,s), 7.34(1H,d,J=7.8Hz),
9.49(1H,br.s), 11.97(1H,br.s).

IR(KBr): ν =3263,3209,3194,3080,1668,1591,1520,1286,1232,1149,106
5 2,750 cm^{-1} .

Example 28

Methyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-
10 chlorobenzaldehyde, 3-aminopyrazole and methyl 3-ketohexanoate
in the same manner as in Example 25.

MP:203-207°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{18}\text{ClN}_3\text{O}_2 \cdot 1/5 \text{H}_2\text{O}$:C,60.88;H,5.53;N,12.53.

Found:C,60.73;H,5.36;N,12.14.

15 MS(EI):331(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.97 (3H,t,J=7.3Hz), 1.64-
1.66(2H,m), 2.72-2.83(2H,m), 3.31(3H,s), 5.57(1H,s),
7.10(1H,d,J=7.3Hz), 7.09-7.11(1H,m), 7.17-7.18(1H,m),
7.27(1H,s), 7.34(1H,d,J=7.8Hz), 9.54(1H,br.s), 11.97(1H,br.s).

20 IR(KBr): ν =3260,3190,1672,1591,1516,1232 cm^{-1} .

Example 29

Ethyl 4-(2-bromophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-bromobenzaldehyde,
25 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner
as in Example 25.

MP:223°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{20}\text{BrN}_3\text{O}_2$:C,55.40;H,5.17;N,10.77.

Found:C,55.08;H,5.14;N,10.85.

30 MS(EI):390(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.86(3H,t,J=7.3Hz),
0.97(3H,t,J=7.3Hz), 1.63-1.69(2H,m), 2.71-2.74(1H,m), 2.80-
2.83(1H,m), 3.77(2H,q,J=7.3Hz), 5.67(1H,s), 7.00(1H,dd,J=7.3Hz

and 7.4Hz), 7.10(1H,d,J=7.3Hz), 7.22(1H,dd,J=7.3Hz and 7.4Hz),
7.28(1H,s), 7.51(1H,d,J=7.3Hz), 9.50(1H,br.s), 11.97(1H,br.s).

Example 30

Ethyl 4,7-dihydro-4-(2-methylphenyl)-6-propyl-2H-pyrazolo[3,4-
5 b]pyridine-5-carboxylate

The title compound was prepared from 2-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:178°C.

10 Anal. Calcd. for: C₁₉H₂₃N₃O₂: C, 70.13; H, 7.12; N, 12.91.

Found: C, 70.12; H, 7.35; N, 12.99.

MS(EI): 325(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.83(3H,t,J=7.3Hz),
0.96(3H,t,J=7.3Hz), 1.62-1.66(2H,m), 2.44(3H,s), 2.64-
15 2.66(1H,m), 2.76-2.79(1H,m), 3.77(2H,q,J=7.3Hz), 5.31(1H,s),
6.93(1H,d,J=7.3Hz), 6.99-7.05(3H,m), 7.18(1H,s), 9.34(1H,br.s),
11.87(1H,br.s).

Example 31

Ethyl 4,7-dihydro-6-propyl-4-(2-trifluoromethylphenyl)-2H-
20 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:198-202°C.

25 Anal. Calcd. for: C₁₉H₂₀F₃N₃O₂ 1/2 H₂O: C, 58.76; H, 5.45; N, 10.81.

Found: C, 58.82; H, 5.92; N, 10.62.

MS(EI): 379(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.76 (3H,t,J=7.3Hz),
0.98(3H,t,J=7.3Hz), 1.64-1.68(2H,m), 2.76-2.79(2H,m),
30 3.80(2H,q,J=7.3Hz), 5.44(1H,s), 7.00(1H,s), 7.27-7.30(1H,m),
7.33(1H,d,J=7.8Hz), 7.53(1H,dd,J=7.3Hz and 7.4Hz),
7.61(1H,d,J=7.3Hz), 9.54(1H,br.s), 11.99(1H,br.s).

IR(KBr): ν=3265, 3198, 2964, 1591, 1514, 1224, 1209, 1093 cm⁻¹.

Example 32

Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:169°C.

Anal. Calcd. for: C₁₉H₂₃N₃O₃: C, 66.84; H, 6.79; N, 12.31.

Found: C, 66.58; H, 6.50; N, 12.34.

10 MS(EI): 341(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.66-1.68(2H, m), 2.66-2.70(1H, m), 2.81-
2.88(1H, m), 3.80(2H, q, J=7.3Hz), 3.85(3H, s), 5.47(1H, s),
6.76(1H, dd, J=7.3Hz and 7.4Hz), 6.89-6.94(2H, m),
15 7.04(1H, dd, J=7.3Hz and 7.4Hz), 7.14(1H, s), 9.29(1H, br.s),
11.82(1H, br.s).

Example 33

Ethyl 4-(2-ethoxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was prepared from 2-ethoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:203°C.

Anal. Calcd. for: C₂₀H₂₅N₃O₃: C, 67.58; H, 7.09; N, 11.82.

25 Found: C, 67.48; H, 7.06; N, 11.81.

MS(EI): 355(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.41(3H, t, J=7.3Hz), 1.64-1.67(2H, m), 2.68-
2.71(1H, m), 2.78-2.81(1H, m), 3.79(2H, q, J=7.3Hz), 4.03-
30 4.05(1H, m), 4.10-4.12(1H, m), 5.48(1H, s), 6.74(1H, dd, J=7.3Hz
and 7.4Hz), 6.87(1H, d, J=7.3Hz), 6.94(1H, d, J=7.3Hz),
7.01(1H, dd, J=7.3Hz and 7.4Hz), 7.14(1H, s), 9.28(1H, br.s),
11.79(1H, br.s).

Example 34Ethyl 4,7-dihydro-4-(2-propoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-propoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:205°C.

Anal. Calcd. for: C₂₁H₂₇N₃O₃: C, 68.27; H, 7.37; N, 11.37.

Found: C, 68.05; H, 7.39; N, 11.35.

10 MS(EI): 369(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.05(3H, t, J=7.3Hz), 1.64-1.67(2H, m), 1.81-
1.84(2H, m), 2.70-2.73(1H, m), 2.78-2.82(1H, m),
3.77(2H, q, J=7.3Hz), 3.92(1H, q, J=7.3Hz), 4.07(1H, q, J=7.3Hz),
15 5.52(1H, s), 6.75(1H, dd, J=7.3Hz and 7.4Hz), 6.88(1H, d, J=7.3Hz),
6.94(1H, d, J=7.3Hz), 7.01(1H, dd, J=7.3Hz and 7.4Hz), 7.11(1H, s),
9.28(1H, br.s), 11.79(1H, br.s).

Example 35Ethyl 4,7-dihydro-4-(2-isopropoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-isopropoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:210°C.

25 Anal. Calcd. for: C₂₁H₂₇N₃O₃: C, 68.27; H, 7.37; N, 11.37.

Found: C, 67.93; H, 7.39; N, 11.32.

MS(EI): 369(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.25(3H, d, J=6.8Hz), 1.39(3H, d, J=6.8Hz),
30 1.64-1.69(2H, m), 2.68-2.72(1H, m), 2.78-2.82(1H, m),
3.77(2H, q, J=7.3Hz), 4.64-4.67(1H, m), 5.45(1H, s),
6.73(1H, dd, J=7.3Hz and 7.4Hz), 6.89-6.90(3H, m), 7.15(1H, s),
9.27(1H, br.s), 11.77(1H, br.s).

Example 36

Ethyl 4-(2-butoxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-butoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:171°C.

Anal. Calcd. for: C₂₂H₂₉N₃O₃: C, 68.90; H, 7.62; N, 10.96.

Found: C, 68.66; H, 7.63; N, 10.89.

10 MS(EI): 383(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.3Hz), 0.95-0.99(6H, m), 1.52-1.80(6H, m), 2.69-2.71(1H, m), 1.76-1.80(1H, m), 3.77(2H, q, J=7.3Hz), 3.95-3.98(1H, m), 4.07-4.10(1H, m), 5.51(1H, s), 6.74(1H, dd, J=7.3Hz and 7.4Hz), 6.88-6.94(2H, m),
15 7.01(1H, dd, J=7.3Hz and 7.4Hz), 7.10(1H, s), 9.28(1H, br.s), 11.79(1H, br.s).

Example 37

Ethyl 4-(2-cyclopentyloxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was prepared from 2-cyclopentyloxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:195°C.

Anal. Calcd. for: C₂₃H₂₉N₃O₃: C, 69.85; H, 7.39; N, 10.62.

25 Found: C, 69.63; H, 7.28; N, 10.61.

MS(EI): 395(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.83(3H, t, J=7.3Hz), 0.97(3H, t, J=7.3Hz), 1.65-1.98(8H, m), 2.66-2.78(2H, m), 3.76(2H, q, J=7.3Hz), 4.89-4.93(1H, m), 5.43(1H, s),
30 6.72(1H, dd, J=7.3Hz and 7.4Hz), 6.88-6.93(2H, m), 7.00(1H, dd, J=7.3Hz and 7.4Hz), 7.10(1H, s), 9.28(1H, br.s), 11.77(1H, br.s).

Example 38

Ethyl 4-(2-benzyloxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-benzyloxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:128°C.

Anal. Calcd. for: C₂₅H₂₇N₃O₃: C, 71.92; H, 6.52; N, 10.06.

Found: C, 71.66; H, 6.73; N, 9.85.

MS(EI): 417(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.64-1.67(2H, m), 2.70-2.73(1H, m), 2.80-
2.83(1H, m), 3.80(2H, q, J=7.3Hz), 5.20(2H, d, J=30Hz), 5.60(1H, s),
6.78(1H, dd, J=7.3Hz and 7.4Hz), 6.96-7.03(3H, m), 7.08(1H, s),
7.35(1H, dd, J=7.3Hz and 7.4Hz), 7.40-7.43(2H, m), 7.52-
7.55(2H, m), 9.30(1H, br.s), 11.79(1H, br.s).

Example 39

Ethyl 4,7-dihydro-4-(2-methylthiophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of 2-methylthiobenzaldehyde (20 g), Meldrum's acid (19 g), ethyl 3-ketohexanoate (21 g) and ammonium acetate (11 g) in acetic acid (130 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give colorless crystals (9.7 g). To a solution of dimethylformamide (1.3 g) in chloroform (5 mL) were added phosphorus oxychloride (1.7 mL) and a solution of the obtained colorless crystals (1.5 g) in chloroform (10 mL) under ice-cooling, and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (18.5 g) solution was added and the mixture was stirred for one hour. The reaction mixture was extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate

(8:2)) to give colorless crystals (0.9 g). To a solution of the obtained colorless crystals (0.9 g) in pyridine (10 mL) was added hydrazine (0.27 g) and the mixture was stirred with heating for 3 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (230 mg) as colorless crystals.

MP:198°C.

10 Anal. Calcd. for: $C_{19}H_{23}N_3O_2S$: C, 63.84; H, 6.49; N, 11.75.

Found: C, 63.56; H, 6.45; N, 11.64.

MS(EI): 357 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.82(3H, t, $J=7.3$ Hz), 0.96(3H, t, $J=7.3$ Hz), 1.62-1.68(2H, m), 2.48(3H, s), 2.67-2.71(1H, m), 2.79-2.83(1H, m), 3.74(2H, q, $J=7.3$ Hz), 5.54(1H, s), 6.99-7.06(3H, m), 7.22-7.25(2H, m), 9.38(1H, br.s), 11.86(1H, br.s).

Example 40

Ethyl 4,7-dihydro-4-(2-methylsulfinylphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of ethyl 4,7-dihydro-4-(2-methylthio)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (100 mg) in tetrahydrofuran (3.0 mL) was added metachloroperbenzoic acid (60 mg) and the mixture was stirred at -78°C for 30 minutes. An aqueous sodium thiosulfate solution was added, and the mixture was extracted with chloroform. The solvent was evaporated under reduced pressure to give colorless crystals. By recrystallization from ethyl acetate, the title compound (50 mg) was obtained as colorless crystals.

30 MP:216°C.

Anal. Calcd. for: $C_{19}H_{23}N_3O_3S$: C, 61.10; H, 6.21; N, 11.25.

Found: C, 61.32; H, 6.18; N, 10.99.

MS(EI): 373 (M^+).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.91(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.64-1.68(2H, m), 2.69-2.72(1H, m),
2.72(3H, s), 2.76-2.79(1H, m), 3.90(2H, q, J=7.3Hz), 5.36(1H, s),
7.15(1H, dd, J=7.3Hz and 7.4Hz), 7.20(1H, s), 7.37-7.39(2H, m),
5 7.85(1H, dd, J=7.3Hz and 7.4Hz), 9.59(1H, br.s), 12.04(1H, br.s).

Example 41

Ethyl 4,7-dihydro-4-(2-nitrophenyl)-6-propyl-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

The title compound was prepared from 2-nitrobenzaldehyde
10 and ethyl 3-ketohexanoate in the same manner as in Example 39.
MP:218°C.

Anal. Calcd. for: C₁₈H₂₀N₄O₄: C, 60.66; H, 5.66; N, 15.72.

Found: C, 60.25; H, 5.65; N, 15.44.

MS(EI): 356(M⁺).

15 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.80(3H, t, J=7.3Hz),
0.95(3H, t, J=7.3Hz), 1.59-1.64(2H, m), 2.69-2.73(1H, m), 2.77-
2.80(1H, m), 3.72(2H, q, J=7.3Hz), 5.45(1H, s), 7.28-7.33(3H, m),
7.56(1H, dd, J=7.3Hz and 7.4Hz), 7.76(1H, d, J=7.3Hz),
9.64(1H, br.s), 10.07(1H, br.s).

Example 42

Ethyl 4-(2-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

The title compound was prepared from 2-cyanobenzaldehyde
and ethyl 3-ketohexanoate in the same manner as in Example 39.
25 MP:211°C.

Anal. Calcd. for: C₁₉H₂₀N₄O₂: C, 67.84; H, 5.99; N, 16.66.

Found: C, 67.49; H, 6.14; N, 16.23.

MS(EI): 336(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.89(3H, t, J=7.3Hz),
30 0.94(3H, t, J=7.3Hz), 1.61-1.67(2H, m), 2.71-2.73(1H, m), 2.79-
2.82(1H, m), 3.80(2H, q, J=7.3Hz), 5.48(1H, s), 7.21-7.29(2H, m),
7.28(1H, dd, J=7.3Hz and 7.4Hz), 7.55(1H, dd, J=7.3Hz and 7.4Hz),
7.70(1H, d, J=7.3Hz), 9.63(1H, br.s), 12.07(1H, br.s).

Example 43

Ethyl 4-(2,3-difluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-difluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:207°C.

Anal. Calcd. for: $C_{18}H_{19}F_2N_3O_2 \cdot 1/5 H_2O$: C, 61.60; H, 5.57; N, 11.97.

Found: C, 61.41; H, 5.56; N, 11.59.

10 MS(EI): 347(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90-0.97(6H, m), 1.60-1.66(2H, m), 2.68-2.71(1H, m), 2.79-2.82(1H, m), 3.83(2H, q, $J=7.3$ Hz), 5.45(1H, s), 6.87(1H, dd, $J=7.3$ Hz and 7.4Hz), 7.03-7.13(2H, m), 7.76(1H, s), 9.55(1H, br.s), 12.03(1H, br.s).

15 **Example 44**

Ethyl 4-(2,3-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-dichlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:220°C.

Anal. Calcd. for: $C_{18}H_{19}Cl_2N_3O_2$: C, 56.85; H, 5.04; N, 11.05.

Found: C, 56.35; H, 5.00; N, 11.01.

MS(EI): 380(M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, $J=7.3$ Hz), 0.99(3H, t, $J=7.3$ Hz), 1.66-1.69(2H, m), 2.74-2.77(1H, m), 2.82-2.86(1H, m), 3.81(2H, q, $J=7.3$ Hz), 5.66(1H, s), 7.10(1H, d, $J=7.3$ Hz), 7.24(1H, dd, $J=7.3$ Hz and 7.4Hz), 7.31(1H, s), 7.38(1H, d, $J=7.3$ Hz), 9.59(1H, br.s), 12.04(1H, br.s).

30 **Example 45**

Ethyl 4-(3-fluoro-2-methylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3-fluoro-2-

methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:159-162°C.

Anal. Calcd. for: C₁₉H₂₂FN₃O₃ 3/10 H₂O: C, 65.42; H, 6.53; N, 12.05.

5 Found: C, 65.56; H, 6.29; N, 12.40.

MS(EI): 343(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89 (3H, t, J=7.3Hz), 0.97 (3H, t, J=7.3Hz), 1.64 (2H, m), 2.36 (3H, s), 2.67-2.84 (2H, m), 3.80 (2H, q, J=7.3Hz), 5.35 (1H, s), 6.86 (2H, d, J=8.8Hz),
10 7.07 (1H, dd, J=7.3Hz and 7.4Hz), 7.23 (1H, s), 9.42 (1H, br.s), 11.94 (1H, br.s).

IR(KBr): ν=3265, 3193, 2966, 2934, 1668, 1591, 1520, 1466, 1240 cm⁻¹.

Example 46

Ethyl 4-(2,3-dimethoxyphenyl)-4,7-dihydro-6-propyl-2H-
15 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-dimethoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:205-206°C.

20 Anal. Calcd. for: C₂₀H₂₅N₃O₄: C, 64.67; H, 6.78; N, 11.31.

Found: C, 64.76; H, 6.81; N, 11.15.

MS(EI): 371(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90 (3H, t, J=7.4Hz), 0.98 (3H, t, J=7.3Hz), 1.66-1.68 (2H, m), 2.68-2.70 (1H, m), 2.80-
25 2.83 (1H, m), 3.77 (3H, s), 3.80 (3H, s), 3.80-3.85 (2H, m), 5.44 (1H, s), 6.58 (1H, d, J=7.3Hz), 6.76 (1H, d, J=6.8Hz), 6.88 (1H, dd, J=7.3Hz and 7.4Hz), 7.11 (1H, s), 9.32 (1H, br.s), 11.83 (1H, br.s).

Example 47

30 Ethyl 4-(2-chloro-3-trifluoromethylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-3-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl 3-

ketohexanoate in the same manner as in Example 25.

MP:236-238°C.

Anal. Calcd. for: C₁₉H₁₉ClF₃N₃O₂: C, 55.15; H, 4.63; N, 10.15.

Found: C, 55.07; H, 4.55; N, 10.13.

5 MS(EI):413(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.82(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.65(2H, m), 2.70-2.90(2H, m), 3.65-
3.85(2H, m), 5.72(1H, s), 7.29(1H, s), 7.41-7.42(2H, m), 7.59-
7.61(1H, m), 9.62(1H, br.s), 12.05(1H, br.s).

10 **Example 48**

Ethyl 4-(2-chloro-4-fluorophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-4-
fluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
15 in the same manner as in Example 25.

MS(EI):363(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.88(3H, t, J=7.3Hz),
0.96(3H, t, J=7.3Hz), 1.62-1.67(2H, m), 2.66-2.80(2H, m),
3.77(2H, q, J=7.3Hz), 5.54(1H, s), 7.08-7.13(2H, m), 7.25(1H, s),
20 7.32(1H, dd, J=2.5Hz and 8.8Hz), 9.53(1H, br.s), 11.99(1H, br.s).

Example 49

Ethyl 4-(2,5-difluorophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,5-
25 difluorobenzaldehyde, 3-aminopyrazole and ethyl 3-
ketohexanoate in the same manner as in Example 25.

MP:168-169°C.

MS(EI):347(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.92-0.99(6H, m), 1.62-1.68(2H, m),
30 2.67-2.71(1H, m), 2.85-2.88(1H, m), 3.80-3.91(2H, m),
4.03(1H, q, J=6.8Hz), 5.40(1H, s), 6.77-6.80(1H, m), 6.98-
7.00(1H, m), 7.12-7.16(1H, m), 7.26(1H, s), 9.59(1H, br.s),
12.06(1H, br.s).

Example 50Ethyl 4-(2,5-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,5-dichlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:162°C.

Anal. Calcd. for: $C_{18}H_{19}Cl_2N_3O_2 \cdot 1/2 H_2O$: C, 55.54; H, 5.18; N, 10.79.

Found: C, 55.50; H, 5.50; N, 11.17.

10 MS(EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=7.3Hz), 0.98(3H, t, J=7.3Hz), 1.62-1.66(2H, m), 2.64-2.67(1H, m), 2.86-2.90(1H, m), 3.81(2H, q, J=7.3Hz), 5.55(1H, s), 7.04(1H, s), 7.18(1H, d, J=7.3Hz), 7.28(1H, s), 7.41(1H, d, J=7.3Hz),

15 9.61(1H, br.s), 12.06(1H, br.s).

Example 51Ethyl 4-(5-fluoro-2-methoxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 5-fluoro-2-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:164-167°C.

Anal. Calcd. for: $C_{19}H_{22}FN_3O_3$: C, 63.50; H, 6.17; N, 11.69.

Found: C, 63.24; H, 6.09; N, 11.70.

25 MS(EI): 359 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87(3H, t, J=7.3Hz), 0.98(3H, t, J=7.3Hz), 1.64-1.69(2H, m), 2.62-2.91(2H, m), 3.79(2H, q, J=7.3Hz), 3.85(3H, s), 5.44(1H, s), 6.33(1H, dd, J=3.0Hz and 7.8Hz), 6.83-6.91(2H, m), 7.17(1H, s), 9.41(1H, br.s),

30 11.89(1H, br.s).

IR(KBr): ν =3252, 2955, 1657, 1510, 1232, 1074 cm^{-1} .

Example 52Ethyl 4-(2-chloro-5-methoxyphenyl)-4,7-dihydro-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-5-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

5 MP:182°C.

Anal. Calcd. for: C₁₉H₂₂ClN₃O₃: C, 60.72; H, 5.90; N, 11.18.

Found: C, 60.58; H, 5.88; N, 11.07.

MS(EI): 375(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H, t, J=7.3Hz),
10 0.99(3H, t, J=7.3Hz), 1.64-1.69(2H, m), 2.64-2.67(1H, m), 2.87-
2.90(1H, m), 3.79(2H, q, J=7.3Hz), 3.86(3H, s), 5.44(1H, s),
6.85(1H, d, J=7.3Hz), 6.94(1H, d, J=7.3Hz), 7.10(1H, dd, J=2.9Hz and
7.3Hz), 7.17(1H, s), 9.43(1H, br.s), 11.91(1H, br.s).

Example 53

15 Ethyl 4-(2,5-dimethoxyphenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,5-dimethoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

20 MP:169-170°C.

MS(EI): 371(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H, t, J=7.3Hz),
0.98(3H, t, J=7.3Hz), 1.68-1.70(2H, m), 2.49-2.54(1H, m), 2.94-
2.97(1H, m), 3.57(3H, s), 3.79-3.83(2H, m), 3.80(3H, s),
25 4.02(1H, q, J=7.3Hz), 5.43(1H, s), 6.49(1H, d, J=2.9Hz),
6.59(1H, dd, J=2.9Hz and 8.8Hz), 6.82(1H, d, J=8.8Hz), 7.14(1H, s),
9.32(1H, br.s), 11.83(1H, br.s).

Example 54

30 Ethyl 4-(2,6-difluorophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,6-difluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:185°C.

Anal. Calcd. for: $C_{18}H_{19}F_2N_3O_2 \cdot 1/2 H_2O$: C, 60.67; H, 5.66; N, 11.79.

Found: C, 60.68; H, 5.46; N, 11.61.

MS(EI): 347 (M^+).

5 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90-0.97(6H, m), 1.54-1.58(2H, m),
2.51-2.54(1H, m), 2.76-2.81(1H, m), 3.82(2H, q, J=7.3Hz),
5.53(1H, s), 6.90(2H, dd, J=7.3Hz and 7.3Hz), 7.16(1H, d, J=7.3Hz),
7.20(1H, s), 9.50(1H, br.s), 11.96(1H, br.s).

Example 55

10 Ethyl 4-(2,6-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,6-dichlorobenzaldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

15 MP:202°C.

Anal. Calcd. for: $C_{18}H_{19}Cl_2N_3O_2 \cdot 3/10 H_2O$: C, 56.06; H, 5.12; N, 10.90.

Found: C, 56.28; H, 5.46; N, 10.78.

MS(EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.83(3H, t, J=7.3Hz),
20 0.92(3H, t, J=7.3Hz), 1.57-1.62(2H, m), 2.47-2.51(1H, m), 2.77-
2.80(1H, m), 3.74(2H, q, J=7.3Hz), 6.03(1H, s), 7.05(1H, s),
7.13(1H, dd, J=7.3Hz and 7.4Hz), 7.22(1H, d, J=7.3Hz),
7.39(1H, d, J=7.3Hz), 9.53(1H, br.s), 11.93(1H, br.s).

Example 56

25 Ethyl 4-(2-chloro-6-fluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-6-fluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

30 MP:180-183°C.

MS(EI): 363 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, J=6.9Hz),
0.94(3H, t, J=7.3Hz), 1.56-1.61(2H, m), 2.50-2.85(2H, m),

3.80(2H,q,J=7.3Hz), 5.75(1H,s), 7.01-7.17(4H,m), 9.52(1H,br.s),
11.97(1H,br.s).

IR(KBr): ν =3265,1591,1518,1456,1228,1097 cm^{-1} .

Example 57

5 Ethyl 4,7-dihydro-6-propyl-4-(pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate dihydrochloride

The title compound was prepared from pyridine-3-aldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39. MP:251°C.

10 Anal. Calcd. for: $\text{C}_{17}\text{H}_{20}\text{N}_4\text{O}_2 \cdot 2\text{HCl}$: C, 52.99; H, 5.76; N, 14.54.

Found: C, 52.99; H, 5.67; N, 14.44.

MS(EI): 312(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.91(3H,t,J=7.3Hz),

1.09(3H,t,J=7.3Hz), 1.52-1.61(2H,m), 2.66-2.71(2H,m), 3.93-

15 4.00(2H,m), 5.24(1H,s), 7.90(1H,dd,J=7.3Hz and 7.4Hz), 8.31-

8.35(2H,m), 8.66-8.69(2H,m), 10.35(1H,br.s).

Example 58

Ethyl 4,7-dihydro-6-propyl-4-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate dihydrochloride

20 The title compound was prepared from pyridine-4-aldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39. MP:266°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{20}\text{N}_4\text{O}_2 \cdot 2\text{HCl}$: C, 52.99; H, 5.76; N, 14.54.

Found: C, 52.63; H, 5.65; N, 14.69.

25 MS(EI): 312(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.91(3H,t,J=7.3Hz),

1.12(3H,t,J=7.3Hz), 1.52-1.59(2H,m), 2.64-2.72(2H,m),

4.01(2H,q,J=7.3Hz), 5.30(1H,s), 7.76(2H,d,J=6.4Hz), 8.66(1H,s),

8.72(2H,d,J=6.4Hz), 10.39(1H,br.s).

30 Example 59

Ethyl 4-(furan-2-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from furan-2-aldehyde,

3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:108-111°C.

MS(EI):301(M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.92(3H, t, J=7.3Hz),
1.05(3H, t, J=6.8Hz), 1.58(2H, q, J=7.3Hz), 2.66-2.72(2H, m),
3.50(3H, br. s), 3.94(2H, q, J=6.8Hz), 5.21(1H, s), 5.78(1H, d,
J=2.9Hz), 6.23(1H, s), 6.24(2H, s), 7.75(1H, s), 7.38(1H, s),
9.42(1H, br. s).

10 IR(KBr):ν=3207, 2962, 1703, 1479, 1348, 1205, 1076, 866cm⁻¹.

Example 60

Ethyl 4-(furan-3-yl)-4,7-dihydro-4-(furan-3-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from furan-3-aldehyde,
15 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:121-123°C.

Anal. Calcd. for: C₁₆H₁₉N₃O₃C₄H₄O₄: C, 57.54; H, 5.55; N, 10.07.

Found: C, 57.14; H, 5.55; N, 10.37.

20 MS(EI):301(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.90(3H, t, J=7.3Hz),
1.08(3H, t, J=7.4Hz), 1.55-1.57(2H, m), 2.62-2.70(2H, m),
3.36(1H, br. s), 3.50(2H, br. s), 3.97(2H, q, J=7.3Hz), 5.06(1H, s),
6.16(1H, s), 6.24(2H, s), 7.13(1H, s), 7.35(1H, s), 7.40(1H, s),
25 9.31(1H, br. s).

IR(KBr):ν=3350, 2972, 1591, 1467, 1361, 1203, 1089cm⁻¹.

Example 61

Ethyl 4,7-dihydro-4-(2-methylfuran-3-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 2-methylfuran-3-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:123-125°C.

Anal. Calcd. for: $C_{17}H_{21}N_3O_3 \cdot 2/5 H_2O$: C, 63.30; H, 6.81; N, 13.03.

Found: C, 63.51; H, 6.64; N, 12.96.

MS(EI): 315 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.93(3H, t, J=7.3Hz),
5 1.08(3H, t, J=7.3Hz), 1.58-1.60(2H, m), 2.20(3H, s), 2.55-
2.75(2H, m), 3.92(2H, q, J=7.3Hz), 4.99(1H, s), 5.96(1H, s),
7.21(2H, s), 9.26(1H, br.s), 11.91(1H, br.s).

IR(KBr): ν =3265, 3198, 2964, 1591, 1514, 1224, 1209, 1093 cm^{-1} .

Example 62

10 Ethyl 4,7-dihydro-6-propyl-4-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from thiophene-2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

15 MP: 129-131°C.

Anal. Calcd. for: $C_{16}H_{19}N_3O_2SC_4H_4O_4 \cdot 1/4 H_2O$: C, 54.85; H, 5.41; N, 9.59.

Found: C, 54.59; H, 5.22; N, 9.97.

MS(EI): 317 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, J=7.4Hz),
20 1.06(3H, t, J=7.3Hz), 1.58-1.60(2H, m), 2.72-2.74(2H, m),
3.50(3H, br.s), 3.94(2H, q, J=7.4Hz), 5.44(1H, s), 6.25(2H, s),
6.69(1H, s), 6.81(1H, d), 7.15(1H, d), 7.37(1H, s), 9.50(1H, br.s).

Example 63

25 Ethyl 4,7-dihydro-4-(3-methylthiophen-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3-methylthiophene-2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 125°C.

30 Anal. Calcd. for: $C_{17}H_{21}N_3O_2S \cdot H_2O$: C, 58.43; H, 6.63; N, 12.02.

Found: C, 58.59; H, 6.33; N, 12.12.

MS(EI): 331 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.96(3H, t, J=7.4Hz),

0.98(3H,t,J=7.3Hz), 1.60-1.63(2H,m), 2.22(3H,s), 2.83-
2.90(2H,m), 3.88(2H,q,J=7.3Hz), 5.42(1H,s), 6.68(1H,d,J=4.9Hz),
7.02(1H,d,J=5.4Hz), 7.29(1H,s), 9.45(1H,br.s), 11.98(1H,br.s).
IR(KBr): ν =3267,3196,2968,1664,1510,1267,1201,1091 cm^{-1} .

5 **Example 64**

Ethyl 4-(5-chlorothiophen-2-yl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 5-chlorothiophene-
2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the
10 same manner as in Example 25.

MP:129-131°C.

Anal. Calcd. for: $\text{C}_{16}\text{H}_{16}\text{N}_3\text{O}_2\text{SC}_4\text{H}_4\text{O}_4$: C, 51.33; H, 4.74; N, 8.98.

Found: C, 51.34; H, 4.54; N, 9.03.

MS(EI): 351(M^+).

15 ^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H,t,J=7.3Hz),
1.10(3H,t,J=6.9Hz), 1.59-1.61(2H,m), 2.57-2.82(2H,m),
3.50(2H,br.s), 3.38(1H,s), 3.98(2H,q,J=6.9Hz), 5.36(1H,s),
6.25(2H,s), 6.53(1H,d,J=3.9Hz), 6.80(1H,d,J=3.4Hz), 7.42(1H,s),
9.60(1H,br.s).

20 IR(KBr): ν =3205,2964,2629,1618,1471,1363,1205,1080,889,652 cm^{-1} .

Example 65

Ethyl 4,7-dihydro-6-propyl-4-(thiophen-3-yl)-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate maleate

The title compound was prepared from thiophene-3-
25 aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the
same manner as in Example 25.

MP:141-143°C.

Anal. Calcd. for: $\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_2\text{SC}_4\text{H}_4\text{O}_4$: C, 54.42; H, 5.35; N, 9.69.

Found: C, 54.17; H, 5.23; N, 9.66.

30 MS(EI): 317(M^+).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H,t,J=7.3Hz),
1.03(3H,t,J=6.8Hz), 1.59-1.61(2H,m), 2.60-2.78(2H,m),
3.50(2H,br.s), 3.91(2H,q,J=6.8Hz), 5.22(2H,s), 6.26(2H,s),

6.84-6.88(2H,m), 7.29(1H,dd,J=3.0Hz and 4.9Hz), 7.33(1H,s),
12.0(1H,br.s).

IR(KBr): ν =3346,2980,2611,1697,1467,1361,1205,1087 cm^{-1} .

Example 66

5 Ethyl 4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from naphthalene-1-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

10 MP:182°C.

Anal. Calcd. for: $\text{C}_{22}\text{H}_{23}\text{N}_3\text{O}_2$:C,73.11;H,6.41;N,11.63.

Found:C,72.95;H,6.47;N,11.40.

MS(EI):361(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.62(3H,t,J=7.3Hz),
15 1.00(3H,t,J=7.3Hz), 1.69-1.73(2H,m), 2.73-2.76(1H,m), 2.84-
2.87(1H,m), 3.67(2H,q,J=7.3Hz), 5.95(1H,s), 7.03(1H,s),
7.23(1H,d,J=7.3Hz), 7.36(1H,dd,J=7.3Hz and 7.4Hz),
7.49(1H,dd,J=7.3Hz and 7.4Hz), 7.57(1H,dd,J=7.3Hz and 7.4Hz),
7.65(1H,d,J=7.3Hz), 7.88(1H,d,J=7.3Hz), 8.40(1H,d,J=7.3Hz),
20 9.45(1H,br.s), 11.82(1H,br.s).

Example 67

Ethyl 4,7-dihydro-4-(naphthalen-2-yl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from naphthalene-2-
25 aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:136-138°C.

Anal. Calcd. for: $\text{C}_{22}\text{H}_{23}\text{N}_3\text{O}_2\cdot\text{C}_4\text{H}_4\text{O}_4$ 1/4 H_2O :C,64.79;H,5.75;N,8.72.

Found:C,64.86;H,5.57;N,8.99.

30 MS(EI):361(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.92-0.98(6H,m), 1.64-1.68(2H,m),
2.72-2.80(2H,m), 3.50(2H,br.s), 3.80(2H,q,J=7.3Hz), 5.27(1H,s),
6.25(2H,s),7.23(1H,s), 7.31(1H,d,J=8.3Hz), 7.41-7.43(2H,m),

7.57(1H,s), 7.73-7.77(2H,m), 9.47(1H,br.s).

IR(KBr): ν =3202,2962,1701,1464,1359,1222 cm^{-1} .

Example 68

Ethyl 4,7-dihydro-4-(2-methoxynaphthalen-1-yl)-6-propyl-2H-
5 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxynaphthalene-1-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:188-191°C.

10 Anal. Calcd. for: $\text{C}_{23}\text{H}_{25}\text{N}_3\text{O}_3 \cdot 2/5 \text{H}_2\text{O}$:C,69.29;H,6.52;N,10.54.

Found:C,69.35;H,6.62;N,10.21.

MS(EI):391(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.71(3H,t,J=7.3Hz),

0.95(3H,t,J=7.3Hz), 1.62-1.63(2H,m), 2.49-2.86(2H,m),

15 3.61(2H,q,J=7.3Hz), 3.97(3H,s), 6.27(1H,s), 6.89(1H,s), 7.16-

7.51(3H,m), 7.71-7.77(2H,m), 7.98(1H,s), 9.43(1H,br.s),

11.77(1H,br.s).

IR(KBr): ν =3258,1655,1593,1082 cm^{-1} .

Example 69

20 Ethyl 4-(2,3-dihydrobenzo[b]furan-7-yl)-4,7-dihydro-6-propyl-
2H- pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-dihydrobenzo[b]furan-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

25 MP:194-196°C.

Anal. Calcd. for: $\text{C}_{20}\text{H}_{23}\text{N}_3\text{O}_3$:C,67.97;H,6.56;N,11.89.

Found:C,67.97;H,6.68;N,11.77.

MS(EI):353(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.92(3H,t,J=7.4Hz),

30 0.97(3H,t,J=7.3Hz), 1.66(2H,m), 2.67-2.70(1H,m), 2.82-

2.84(1H,m), 3.15(2H,t,J=8.8Hz), 3.83-3.86(2H,m), 4.55-

4.58(2H,m), 5.29(1H,s), 6.64(1H,dd,J=7.3Hz and 7.4Hz),

6.72(1H,d,J=6.9Hz), 6.93(1H,dd,J=7.3Hz and 7.4Hz), 7.20(1H,s),

9.32(1H,br.s), 11.86(1H,br.s).

Example 70

Ethyl 4-(5-bromo-2,3-dihydrobenzo[b]furan-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 The title compound was prepared from 5-bromo-2,3-dihydrobenzo[b]furan-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:200-210°C.

Anal. Calcd. for: C₂₀H₂₂BrN₃O₃: C, 55.57; H, 5.13; N, 9.72.

10 Found: C, 55.23; H, 5.09; N, 9.89.

MS(EI): 432(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.93-0.98(6H,m),

1.64(2H,q,J=7.3Hz), 2.63(1H,m), 2.88-2.90(1H,m),

3.16(2H,t,J=8.3Hz), 3.85-3.87(2H,m), 4.57-4.60(2H,m),

15 5.23(1H,s), 6.78(1H,s), 7.11(1H,s), 7.22(1H,s), 9.44(1H,br.s),

11.94(1H,br.s).

Example 71

Ethyl 4-(5-chloro-2,3-dihydro-2-methylbenzo[b]furan-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 maleate

The title compound was prepared from 5-chloro-2,3-dihydro-2-methylbenzo[b]furan-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:155-158°C.

25 Anal. Calcd. for: C₂₁H₂₄N₃O₃C₄H₄O₄: C, 57.95; H, 5.45; N, 8.11.

Found: C, 57.57; H, 5.28; N, 8.47.

MS(EI): 401(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(6H,t,J=6.8Hz),

1.03(3H,d,J=6.3Hz), 1.65(2H,m), 2.40-2.73(2H,m), 2.87(1H,m),

30 3.29(1H,m), 3.50(3H,br.s), 3.84(2H,q,J=6.8Hz), 5.05(1H,m),

5.23(1H,s), 6.25(2H,s), 6.64(1H,s), 6.95(1H,s),

7.20(1H,d,J=4.4Hz), 9.43(1H,br.s).

IR(KBr): ν=3207, 2976, 1589, 1462, 1201, 1082cm⁻¹.

Example 72

Ethyl 4-(2H-1-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2H-1-benzopyran-8-
5 aldehyde and ethyl 3-ketohexanoate in the same manner as in
Example 39.

MP:194°C.

Anal. Calcd. for: $C_{21}H_{23}N_3O_3$: C, 69.02; H, 6.34; N, 11.50.

Found: C, 68.60; H, 6.43; N, 11.25.

10 MS(EI): 194 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90(3H, t, J=7.3Hz),
0.96(3H, t, J=7.3Hz), 1.64-1.68(2H, m), 2.62-2.66(1H, m), 2.80-
2.84(1H, m), 3.81(2H, q, J=7.3Hz), 4.85(2H, dd, J=2.0Hz and 9.8Hz),
5.39(1H, s), 5.89(1H, d, J=9.8Hz), 6.46(1H, d, J=9.8Hz), 6.67-
15 6.80(3H, m), 7.18(1H, s), 9.31(1H, br. s), 11.86(1H, br. s).

Example 73

Ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3,4-dihydro-2H-
20 benzopyran-8-aldehyde and ethyl 3-ketohexanoate in the same
manner as in Example 39.

MP:208°C.

Anal. Calcd. for: $C_{21}H_{25}N_3O_3 \cdot 1/2 H_2O$: C, 67.01; H, 6.96; N, 11.16.

Found: C, 67.41; H, 6.84; N, 10.93.

25 MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.63-1.68(2H, m), 1.92-1.96(2H, m), 2.67-
2.82(4H, m), 3.80(2H, q, J=7.3Hz), 4.22-4.26(2H, m), 5.41(1H, s),
6.61(1H, dd, J=7.3Hz and 7.4Hz), 6.71-6.75(2H, m), 7.17(1H, s),
30 9.25(1H, br. s), 11.80(1H, br. s).

Example 74

Ethyl 4,7-dihydro-6-propyl-4-(quinolin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from quinoline-4-aldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:198°C.

5 Anal. Calcd. for: $C_{21}H_{22}N_4O_2 \cdot 2/5 H_2O$: C, 68.24; H, 6.22; N, 15.16.

Found: C, 68.39; H, 6.04; N, 14.83.

MS(EI): 362 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.61(3H, t, J=7.3Hz),
1.02(3H, t, J=7.3Hz), 1.68-1.72(2H, m), 2.76-2.78(1H, m), 2.86-
10 2.89(1H, m), 3.66-3.68(2H, m), 5.97(1H, s), 7.07(1H, s),
7.17(1H, d, J=4.4Hz), 7.65(1H, dd, J=7.3Hz and 7.4Hz),
7.74(1H, dd, J=7.3Hz and 7.4Hz), 7.99(1H, d, J=7.3Hz),
8.48(1H, d, J=7.8Hz), 8.73(1H, d, J=4.4Hz), 9.61(1H, br.s),
11.94(1H, br.s).

15 **Example 75**

Ethyl 4-(benzo[b]thiophen-3-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from benzo[b]thiophene-3-aldehyde and ethyl 3-ketohexanoate in the same manner as in
20 Example 39.

MP:222°C.

Anal. Calcd. for: $C_{20}H_{21}N_3O_2S$: C, 65.37; H, 5.76; N, 11.44.

Found: C, 65.11; H, 5.31; N, 11.83.

MS(EI): 238 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.64(3H, t, J=7.3Hz),
1.20(3H, t, J=7.3Hz), 1.56-1.58(2H, m), 2.66-2.78(2H, m),
4.11(2H, q, J=7.3Hz), 4.89(1H, s), 7.42-7.50(2H, m), 7.55(1H, s),
7.61(1H, s), 7.96-8.01(2H, m), 10.32(1H, br.s), 12.13(1H, br.s).

Example 76

30 Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-

ketohehexanoate in the same manner as in Example 39.

MP:207°C.

Anal. Calcd. for: C₁₈H₁₉N₅O₃: C, 61.18; H, 5.42; N, 19.82.

Found: C, 61.06; H, 5.50; N, 19.66.

5 MS(EI): 353(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.77(3H, t, J=7.3Hz),

0.97(3H, t, J=7.3Hz), 2.72-2.77(1H, m), 2.82-2.86(1H, m),

3.79(2H, q, J=7.3Hz), 5.68(1H, s), 7.11(1H, d, J=7.3Hz), 7.22(1H, s),

7.51(1H, dd, J=7.3Hz and 7.4Hz), 7.78(1H, d, J=7.3Hz),

10 9.66(1H, br.s), 12.01(1H, br.s).

Example 77

Ethyl 4-(1,3-benzdioxazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 1,3-benzdioxazole-
15 4-aldehyde, 3-aminopyrazole and ethyl 3-ketohehexanoate in the same manner as in Example 25.

MP:203-207°C.

Anal. Calcd. for: C₁₉H₂₁N₃O₄ 1/10 H₂O: C, 63.89; H, 5.98; N, 11.76.

Found: C, 63.72; H, 5.86; N, 12.01.

20 MS(EI): 355(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz),

0.96(3H, t, J=7.4Hz), 1.61-1.67(2H, m), 2.64-2.82(2H, m), 3.80-

3.88(2H, m), 5.28(1H, s), 5.99(1H, s), 6.00(1H, d, J=9.7Hz),

6.50(1H, d, J=5.9Hz), 6.65(1H, s), 6.65-6.69(1H, m), 7.25(1H, s),

25 9.40(1H, br.s), 11.94(1H, br.s).

IR(KBr): ν=3265, 3188, 2962, 1662, 1587, 1514, 1462, 1253, 1215, 1066cm⁻¹.

Example 78

Ethyl 4-(6-chloro-3,4-dihydro-2,2-dimethyl-2H-1,4-benzoxazin-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-
30 carboxylate maleate

The title compound was prepared from 6-chloro-3,4-dihydro-2,2-dimethyl-2H-1,4-benzoxazine-8-aldehyde, 3-aminopyrazole and ethyl 3-ketohehexanoate in the same manner as

in Example 25.

MS(EI): 430 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, $J=7.4\text{Hz}$),
0.96(3H, t, $J=7.3\text{Hz}$), 1.18(3H, s), 1.32(3H, s), 1.62-1.64(2H, m),
5 2.66-2.82(2H, m), 2.99(2H, s), 3.80(2H, t, $J=7.3\text{Hz}$), 5.32(1H, s),
6.01(2H, s), 6.14(1H, s), 6.32(1H, s), 7.14(1H, s), 9.31(1H, br. s),
11.82(1H, br. s).

IR(KBr): $\nu=3281, 2974, 1672, 1599, 1520, 1207, 1155, 1091\text{cm}^{-1}$.

Example 79

10 Ethyl 4-(6-chloro-3,4-dihydro-2,2,4-trimethyl-1,4-benzoxazin-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 6-chloro-3,4-dihydro-2,2,4-trimethyl-2H-1,4-benzoxazine-8-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as
15 in Example 25.

MS(EI): 444 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, $J=7.3\text{Hz}$),
0.96(3H, t, $J=7.3\text{Hz}$), 1.20(6H, s), 1.35(3H, s), 1.63-1.65(2H, m),
20 2.83(2H, s), 3.00(2H, q, $J=7.3\text{Hz}$), 5.34(1H, s), 6.26(2H, s),
6.43(1H, d, $J=2.5\text{Hz}$), 7.13(1H, s), 9.33(1H, s), 11.82(1H, br. s).

IR(KBr): $\nu=3273, 2974, 1666, 1597, 1518, 1458, 1259, 1211\text{cm}^{-1}$.

Example 80

25 Ethyl 4-(2,3-dihydro-1,4-benzodioxin-6-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 2,3-dihydro-1,4-benzodioxin-6-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 147-149°C.

30 Anal. Calcd. for: $\text{C}_{20}\text{H}_{23}\text{N}_3\text{O}_4\text{C}_4\text{H}_4\text{O}_4$: C, 59.37; H, 5.60; N, 8.66.

Found: C, 59.12; H, 5.63; N, 8.57.

MS(EI): 369 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.93(3H, t, $J=7.3\text{Hz}$),

- 1.02(3H,t,J=6.8Hz), 1.60(2H,q,J=7.3Hz), 2.64-2.68(2H,m),
3.50(2H,br.s), 3.86(2H,q,J=7.3Hz), 4.14(4H,s), 4.99(1H,s),
6.26(2H,s), 6.54(1H,s), 6.57(1H,d,J=7.8Hz), 6.65(1H,d,J=7.8Hz),
7.21(1H,s), 11.97(1H,br.s).
- 5 IR(KBr): ν =3211,2694,2878,2658,1697,1506,1466,1363,1302,1082 cm^{-1} .

Example 81

Ethyl 4-(benzo[b]furan-2-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

- The title compound was prepared from benzo[b]furan-2-
10 aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the
same manner as in Example 25.

MP:123-125°C.

Anal. Calcd. for: $\text{C}_{20}\text{H}_{21}\text{N}_3\text{O}_3\text{C}_4\text{H}_4\text{O}_4 \cdot 1/2 \text{H}_2\text{O}$:C,61.19;H,5.43;N,8.92.

Found:C,61.02;H,5.41;N,9.27.

- 15 MS(EI):351(M^+).

$^1\text{H-NMR}$ (400MHz,DMSO- d_6) δ (ppm): 0.96(3H,t,J=7.3Hz),
1.02(3H,t,J=6.8Hz), 1.63(2H,q,J=7.3Hz), 2.73-2.76(2H,m),
3.50(3H,br.s), 3.93(2H,q,J=7.3Hz), 5.36(1H,s), 6.24(2H,s),
6.43(1H,s), 7.10-7.21(2H,m), 7.41-7.48(3H,m), 9.51(1H,br.s).

- 20 IR(KBr): ν =3190,3080,2962,1705,1581,1454,1359,1195,883 cm^{-1} .

Example 82

Ethyl 4-(2-chlorophenyl)-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

- The title compound was prepared from 2-
25 chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketopentanoate
in the same manner as in Example 1.

MP:213°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{18}\text{ClN}_3\text{O}_2$:C,61.54;H,5.47;N,12.66.

Found:C,61.54;H,5.46;N,12.68.

- 30 MS(EI):331(M^+).

$^1\text{H-NMR}$ (400MHz,DMSO- d_6) δ (ppm): 0.85(3H,t,J=7.3Hz),
1.21(3H,t,J=7.3Hz), 2.78-2.84(2H,m), 3.78(2H,q,J=7.3Hz),
5.58(1H,s), 7.07-7.12(2H,m), 7.18(1H,dd,J=7.3Hz and

7.4Hz), 7.25(1H,s), 7.34(1H,d,J=7.3Hz), 9.52(1H,br.s),
11.97(1H,br.s).

Example 83

Ethyl 6-butyl-4-(2-chlorophenyl)-4,7-dihydro-2H-pyrazolo[3,4-
5 b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 1.

MP:209°C.

10 Anal. Calcd. for: C₁₉H₂₂ClN₃O₂ 1/5 H₂O: C, 62.79; H, 6.21; N, 11.56.
Found: C, 62.78; H, 6.11; N, 11.45.

MS(EI): 359(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H,t,J=7.3Hz),
0.92(3H,t,J=7.3Hz), 1.36-1.42(2H,m), 1.60-1.64(2H,m), 2.72-
15 2.76(1H,m), 2.83-2.86(1H,m), 3.78(2H,q,J=7.3Hz), 5.58(1H,s),
7.07-7.11(2H,m), 7.18(1H,dd,J=7.3Hz and 7.4Hz), 7.24(1H,s),
7.34(1H,d,J=7.3Hz), 9.49(1H,br.s), 11.96(1H,br.s).

Example 84

Methyl 4-(2-chlorophenyl)-4,7-dihydro-6-methoxymethyl-2H-
20 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and methyl 4-methoxyacetoacetate in the same manner as in Example 1.

MP:160°C.

25 Anal. Calcd. for: C₁₆H₁₆ClN₃O₃: C, 57.33; H, 4.83; N, 12.59.
Found: C, 57.53; H, 4.86; N, 12.58.

MS(EI): 333(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.36(3H,s), 3.38(3H,s),
4.67(2H,s), 5.58(1H,s), 7.08-7.13(2H,m), 7.19(1H,dd,J=7.3Hz
30 and 7.4Hz), 7.32-7.36(2H,m), 9.14(1H,br.s), 12.08(1H,br.s).

Example 85

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl benzoylacetoacetate in the same manner as in Example 1.

MP:214°C.

5 Anal. Calcd. for: $C_{21}H_{18}ClN_3O_2 \cdot 3/10 H_2O$: C, 65.47; H, 4.87; N, 10.91.

Found: C, 65.29; H, 4.73; N, 10.93.

MS(EI): 379 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.57(3H, t, J=7.3Hz),
3.52(2H, q, J=7.3Hz), 5.65(1H, s), 7.14(1H, dd, J=7.3Hz and 7.4Hz),
10 7.27(1H, dd, J=7.3Hz and 7.4Hz), 7.37-7.40(8H, m), 9.53(1H, br.s),
12.04(1H, br.s).

Example 86

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl (4-methoxybenzoyl)acetate in the same manner as in Example 1.

MP:211°C.

Anal. Calcd. for: $C_{22}H_{20}ClN_3O_3$: C, 64.47; H, 4.92; N, 10.25.

20 Found: C, 64.30; H, 5.00; N, 10.24.

MS(EI): 409 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.64(3H, t, J=7.3Hz),
3.56(2H, q, J=7.3Hz), 3.79(3H, s), 5.63(1H, s), 6.95(2H, d, J=7.3Hz),
7.13(1H, dd, J=7.3Hz and 7.4Hz), 7.24-7.38(6H, m), 9.45(1H, br.s),
25 12.03(1H, br.s).

Example 87

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl (thiophen-2-carbonyl)acetate in the same manner as in Example 1.

MP:200°C.

Anal. Calcd. for: $C_{19}H_{16}ClN_3O_2S$: C, 59.14; H, 4.18; N, 10.89.

Found: C, 59.04; H, 4.31; N, 11.14.

MS(EI): 385(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.02(3H, t, J=7.3Hz),
4.04(2H, q, J=7.3Hz), 5.16(1H, s), 6.58(1H, d, J=7.3Hz), 7.18-
5 7.70(7H, m), 9.60(1H, br.s), 12.74(1H, br.s).

Example 88

Ethyl 6-benzyl-4-(2-chlorophenyl)-4,7-dihydro-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

The title compound was prepared from 2-
10 chlorobenzaldehyde, 3-aminopyrazole and ethyl 4-
phenylacetoacetate in the same manner as in Example 1.

MP: 247°C.

Anal. Calcd. for: C₂₂H₂₀ClN₃O₂ 1/5 H₂O: C, 66.48; H, 5.17; N, 10.57.

Found: C, 66.30; H, 5.17; N, 10.37.

15 MS(EI): 393(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.81(3H, t, J=7.3Hz),
3.76(2H, q, J=7.3Hz), 4.25(2H, s), 5.65(1H, s), 7.06-7.41(10H, m),
9.68(1H, br.s), 12.01(1H, br.s).

Example 89

20 Ethyl 6-ethyl-4,7-dihydro-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

The title compound was prepared from 2-
methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-
ketopentanoate in the same manner as in Example 1.

25 MP: 169°C.

Anal. Calcd. for: C₁₈H₂₁N₃O₃ 3/10 H₂O: C, 64.97; H, 6.54; N, 12.63.

Found: C, 64.86; H, 6.84; N, 12.33.

MS(EI): 327(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=7.3Hz),
30 1.18(3H, t, J=7.3Hz), 2.73-2.76(1H, m), 2.81-2.85(1H, m),
3.74(2H, q, J=7.3Hz), 3.85(3H, s), 5.46(1H, s), 6.76(1H, dd, J=7.3Hz
and 7.4Hz), 6.89-6.94(2H, m), 7.04(1H, dd, J=7.3Hz and 7.4Hz),
7.14(1H, s), 9.32(1H, br.s), 11.82(1H, br.s).

Example 90Ethyl 6-butyl-4,7-dihydro-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 1.

MP:190°C.

Anal. Calcd. for: $C_{20}H_{25}N_3O_3 \cdot 1/2 H_2O$: C, 65.91; H, 7.19; N, 11.53.

Found: C, 65.92; H, 7.07; N, 11.88.

10 MS(EI): 355(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.85(3H, t, J=7.3Hz),
0.93(3H, t, J=7.3Hz), 1.38-1.44(2H, m), 1.59-1.64(2H, m), 2.64-
2.68(1H, m), 2.85-2.90(1H, m), 3.81(2H, q, J=7.3Hz), 3.85(3H, s),
5.47(1H, s), 6.76(1H, dd, J=7.3Hz and 7.4Hz), 6.89-6.94(2H, m),
15 7.04(1H, dd, J=7.3Hz and 7.4Hz), 7.14(1H, s), 9.29(1H, br.s),
11.82(1H, br.s).

Example 91Methyl 4,7-dihydro-6-methoxymethyl-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and methyl 4-methoxyacetoacetate in the same manner as in Example 1.

MP:186°C.

Anal. Calcd. for: $C_{17}H_{19}N_3O_4 \cdot 1/5 H_2O$: C, 61.32; H, 5.87; N, 12.62.

25 Found: C, 61.34; H, 5.84; N, 12.52.

MS(EI): 329(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.36(3H, s), 3.38(3H, s),
3.86(3H, s), 4.68(2H, s), 5.46(1H, s), 6.77(1H, dd, J=7.3Hz and
7.4Hz), 6.90-6.94(2H, m), 7.06(1H, dd, J=7.3Hz and 7.4Hz),
30 7.22(1H, s), 8.94(1H, br.s), 11.94(1H, br.s).

Example 92Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl benzoylacetate in the same manner as in Example 1.

MP:195°C.

5 Anal. Calcd. for: C₂₂H₂₁N₃O₃: C, 70.38; H, 5.64; N, 11.19.

Found: C, 70.41; H, 5.71; N, 11.27.

MS(EI): 375(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.55(3H, t, J=7.3Hz),
3.53(2H, q, J=7.3Hz), 3.88(3H, s), 5.52(1H, s), 6.84(1H, dd, J=7.3Hz
10 and 7.4Hz), 6.94(1H, d, J=7.3Hz), 7.09(1H, dd, J=7.3Hz and 7.4Hz),
7.18(1H, d, J=7.3Hz), 7.23(1H, s), 7.37-7.40(5H, m), 9.33(1H, br.s),
11.90(1H, br.s).

Example 93

4-(2-Chlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-
15 pyrazolo[3,4-b]pyridine

To an aqueous solution (50 mL) of nitromethane (50 g) was added an aqueous solution (50 mL) of n-butylaldehyde (59 g), and the mixture was stirred with heating at 60°C for 6 hours. The reaction mixture was allowed to cool to ambient
20 temperature, and extracted with ethyl acetate. The solvent was evaporated under reduced pressure to give a brown oil (58 g). To a mixed solution of the obtained oil (50 g) in water (50 mL) and acetone (50 mL) was added sodium chromate (70 g). Under ice-cooling, concentrated sulfuric acid (46 mL) was
25 added dropwise and the mixture was stirred for 5 hours. Ice-water (200 mL) was added and the mixture was extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give
30 1-nitropentan-2-one (40 g) as a brown oil. A solution of 2-chlorobenzaldehyde (1.8 g), 3-aminopyrazole (1.0 g) and 1-nitropentan-2-one (1.4 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to

room temperature, and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (680 mg) as yellow crystals.

5 MP:228°C.

Anal. Calcd. for: $C_{15}H_{15}ClN_4O_2$: C, 56.52; H, 4.74; N, 17.58.

Found: C, 56.26; H, 4.91; N, 17.64.

MS(EI): 318 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.02(3H, t, J=7.3Hz), 1.70-
10 1.73(2H, m), 2.89-2.91(1H, m), 2.99-3.02(1H, m), 5.90(1H, s),
7.09-7.21(3H, m), 7.39(1H, d, J=7.3Hz), 7.44(1H, s),
10.84(1H, br.s), 12.43(1H, br.s).

Example 94

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-
15 pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (4.8 g) in THF (150 mL) was added n-BuLi (67 mmol) at -78°C. Further, methyl butanoate (10 g) was added and the mixture was stirred for one hour. After acidification with hydrochloric acid, the mixture was
20 extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give 1-cyanopentan-2-one (5.5 g) as a colorless oil. A solution of 2-chlorobenzaldehyde (1.9 g), 3-aminopyrazole (1.0
25 g) and 1-cyanopentan-2-one (1.6 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated crystals were collected by filtration to give the title compound (1.3 g) as colorless crystals.

30 MP:248°C.

Anal. Calcd. for: $C_{16}H_{15}ClN_4$: C, 64.32; H, 5.06; N, 18.75.

Found: C, 64.49; H, 5.18; N, 18.81.

MS(EI): 298 (M^+).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.95(3H, t, J=7.3Hz), 1.64-1.70(2H, m), 2.38-2.42(2H, m), 5.36(1H, s), 7.23-7.26(3H, m), 7.32(1H, dd, J=7.3Hz and 7.4Hz), 7.42(1H, d, J=7.3Hz), 9.83(1H, br.s), 12.15(1H, br.s).

5 **Example 95**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (76 g) in DMSO (100 mL) was added methyl p-anisate (100 g) and the mixture was stirred
10 with heating at 60°C for one hour. The reaction mixture was allowed to cool, and cold water (500 mL) was added dropwise. The mixture was acidified with hydrochloric acid and the precipitated crystals were collected by filtration. The obtained crystals were extracted with ethyl acetate and the
15 solvent was evaporated under reduced pressure. The residue was recrystallized from ethyl acetate to give benzoylacetonitrile (60 g) as colorless crystals. A solution of 2-chlorobenzaldehyde (1.7 g), 3-aminopyrazole (1.0 g) and benzoylacetonitrile (1.8 g) in acetonitrile (20 mL) was heated
20 under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated crystals were collected by filtration to give the title compound (2.63 g) as colorless crystals.

MP:124°C.

25 Anal. Calcd. for: C₂₀H₁₅ClN₄O 8/5 H₂O: C, 61.34; H, 4.68; N, 14.31.

Found: C, 61.32; H, 4.88; N, 14.31.

MS(EI): 362(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 3.81(3H, s), 5.48(1H, s), 7.04(2H, d, J=7.3Hz), 7.26(1H, dd, J=7.3Hz and 7.4Hz), 7.32(1H, s),
30 7.35-7.39(4H, m), 7.45(1H, d, J=7.3Hz), 9.99(1H, br.s), 12.22(1H, br.s).

Example 96

4-(2-Chlorophenyl)-2,4,7,8-tetrahydrofurano[3,4-

b]pyrazolo[4,3-e]pyridin-5-one

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 4-chloroacetoacetate in the same manner as in Example 1.

5 MP:>270°C.

Anal. Calcd. for: $C_{14}H_{10}ClN_3O_2 \cdot 2/5 H_2O$: C, 57.02; H, 3.69; N, 14.25.

Found: C, 57.13; H, 3.39; N, 14.38.

MS (FAB): 288 ($M^+ + 1$).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 4.91(2H, dd, J=5.6Hz and 26.6Hz),
10 5.34(1H, s), 7.15-7.24(3H, m), 7.34(1H, s), 7.41(1H, d, J=6.8Hz),
10.31(1H, br.s), 12.20(1H, br.s).

IR(KBr): ν =3167, 2966, 1722, 1637, 1608, 1510, 1026 cm^{-1} .

Example 97

5'-Ethoxycarbonyl-4',7'-dihydro-6'-propyl-
15 spiro[benzo[b]thiophene-3(2H),4'-2'H-pyrazolo[3,4-b]pyridine]-
5-oxide

A solution of 2-methylthiobenzaldehyde (62 g), Meldrum's acid (58.7 g), ethyl 3-ketohexanoate (64.4 g) and ammonium acetate (40 g) in acetic acid (400 mL) was heated under reflux
20 overnight. After the solution was cooled to room temperature, the solvent was evaporated under reduced pressure to give colorless crystals (40.2 g). To a solution of dimethylformamide (26.3 g) in chloroform (100 mL) were added, under ice-cooling, phosphorus oxychloride (33.6 mL) and a
25 solution of the obtained colorless crystals (30 g) in chloroform (200 mL), and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (370 g) solution was added and the mixture was stirred for one hour. The reaction mixture was extracted with chloroform and the solvent
30 was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give colorless crystals. To a solution of the obtained crystals in acetone (500 mL) was

added diammonium cerium nitrate (42 g) and the mixture was stirred for 30 minutes. The solvent was evaporated under reduced pressure and the residue was extracted with ethyl acetate. The solvent was evaporated under reduced pressure to
5 give colorless crystals. To a solution of the obtained colorless crystals in tetrahydrofuran (500 mL) was added metachloroperbenzoic acid (12 g) at -78°C and the mixture was stirred for 30 minutes. An aqueous sodium thiosulfate solution was added, and the mixture was extracted with chloroform. The
10 solvent was evaporated under reduced pressure to give colorless crystals. By recrystallization from ethyl acetate, colorless crystals (15 g) were obtained. To a solution of the obtained colorless crystals in tetrahydrofuran (100 mL) was added lithium diisopropylamide (2.5 eq.) at -78°C. Immediately
15 thereafter, methanol and an aqueous ammonium chloride solution were added. The mixture was extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. To a solution of the obtained oil in pyridine (50 mL) was added hydrazine (4.2 g) and the mixture was stirred with
20 heating for 2 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give title compound (0.8 g) as colorless crystals.

25 MP:246°C.

Anal. Calcd. for: $C_{19}H_{21}N_3O_3S$: C, 61.44; H, 5.70; N, 11.31.

Found: C, 61.58; H, 5.81; N, 11.16.

MS(EI): 371 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.70(3H, t, J=7.3Hz),
30 0.96(3H, t, J=7.3Hz), 1.63-1.68(2H, m), 2.67-2.76(2H, m),
3.07(1H, d, J=14.9Hz), 3.64(2H, q, J=7.3Hz), 4.00(1H, d, J=14.9Hz),
7.05-7.09(2H, m), 7.40(1H, dd, J=7.3Hz and 7.4Hz),
7.50(1H, dd, J=7.3Hz and 7.4Hz), 7.81(1H, d, J=7.3Hz),

9.83(1H,br.s), 12.11(1H,br.s).

Example 98

Ethyl 4,7-dihydro-4-(2-hydroxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 A solution of 2-methoxybenzaldehyde (15 g), Meldrum's acid (16 g), ethyl 3-ketohexanoate (17.4 g) and ammonium acetate (9.4 g) in acetic acid (110 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced
10 pressure to give colorless crystals (8.0 g). To a solution of the obtained colorless crystals (5.2 g) in dichloromethane (150 mL) were added ethanedithiol (20 mL) and aluminum chloride (32 g), and the mixture was stirred for 2 hours. After neutralization with 1N aqueous sodium hydroxide solution,
15 the mixture was extracted with chloroform. The solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give colorless crystals (2.0 g). To a solution of dimethylformamide (1.9 g) in chloroform (10
20 mL) were added phosphorus oxychloride (2.5 mL) and a solution of the obtained crystals in chloroform (20 mL) under ice-cooling, and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (27 g) solution was added and the mixture was stirred for one hour. The mixture was
25 extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give a colorless oil (1.4 g). To a solution of the obtained oil in pyridine (10 mL) was added hydrazine
30 (0.7 g), and the mixture was stirred with heating for 2 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column

chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (0.2 g) as colorless crystals.

MP:177°C

Anal. Calcd. for: $C_{18}H_{21}N_3O_3$: C, 66.04; H, 6.47; N, 12.84.

5 Found: C, 65.96; H, 6.21; N, 12.66.

MS(EI): 327 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.80 (3H, t, J=7.3Hz),
0.96 (3H, t, J=7.3Hz), 1.56-1.59 (2H, m), 2.70-2.80 (2H, m),
3.76 (2H, q, J=7.3Hz), 5.50 (1H, s), 7.28-7.33 (3H, m),
10 7.63 (1H, dd, J=7.3Hz and 7.4Hz), 7.76 (1H, d, J=7.3Hz),
9.64 (1H, br.s), 9.68 (1H, br.s), 10.12 (1H, br.s).

Example 99

Ethyl 4-(2-aminophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

15 To a solution of ethyl 4,7-dihydro-4-(2-nitrophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (1.68 g) in methanol (30 mL) was added 5% palladium-carbon (500 mg), and the mixture was stirred under 10 atm for 3 hours. After removing palladium-carbon by Celite filtration, the solvent
20 was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (120 mg) as colorless crystals.

MP:179°C.

25 Anal. Calcd. for: $C_{18}H_{22}N_4O_2$: C, 66.24; H, 6.79; N, 17.17.

Found: C, 65.96; H, 6.62; N, 17.16.

MS(EI): 326 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.82 (3H, t, J=7.3Hz),
0.98 (3H, t, J=7.3Hz), 1.58-1.64 (2H, m), 2.72-2.78 (2H, m),
30 3.78 (2H, q, J=7.3Hz), 5.52 (1H, s), 6.35-6.38 (2H, br.s), 7.28-
7.36 (3H, m), 7.58 (1H, dd, J=7.3Hz and 7.4Hz), 7.78 (1H, d, J=7.3Hz),
9.58 (1H, br.s), 11.48 (1H, br.s).

Example 100

Ethyl 4-(2-ethylphenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-ethylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner
5 as in Example 25.

MP:186°C.

Anal. Calcd. for: $C_{20}H_{25}N_3O_2 \cdot 1/5 H_2O$: C, 70.03; H, 7.46; N, 12.25.

Found: C, 69.91; H, 7.53; N, 11.98.

MS(EI): 339 (M^+).

10 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.86(3H, t, J=7.3Hz),
0.94(3H, t, J=7.3Hz), 1.24(3H, t, J=7.3Hz), 1.64(2H, q, J=7.3Hz),
2.64-2.68(1H, m), 2.77-2.86(3H, m), 3.78(2H, q, J=7.3Hz),
5.34(1H, s), 6.98-7.01(3H, m), 7.07-7.10(2H, m), 9.34(1H, s),
11.89(1H, s).

15 **Example 101**

Ethyl 4,7-dihydro-6-propyl-4-(2-propylphenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-propylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
20 in the same manner as in Example 25.

MP:197°C.

Anal. Calcd. for: $C_{21}H_{27}N_3O_2$: C, 71.36; H, 7.70; N, 11.89.

Found: C, 71.07; H, 7.73; N, 11.84.

MS(EI): 353 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87(3H, t, J=7.3Hz), 0.94-
1.00(6H, m), 1.64(2H, q, J=7.3Hz), 2.68-2.80(4H, m),
3.79(2H, q, J=7.3Hz), 5.33(1H, s), 6.98-7.06(5H, m), 9.34(1H, s),
11.88(1H, s).

Example 102

30 Ethyl 4-(2-butylphenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-butylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner

as in Example 25.

MP:175°C.

Anal. Calcd. for: C₂₂H₂₉N₃O₂: C, 71.90; H, 7.95; N, 11.43.

Found: C, 71.50; H, 7.94; N, 11.36.

5 MS(EI): 367(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.3Hz), 0.92-0.97(6H, m), 1.40(2H, q, J=7.3Hz), 1.60-1.66(4H, m), 2.70-2.82(4H, m), 3.80(2H, q, J=7.3Hz), 5.33(1H, s), 6.97-7.06(5H, m), 9.34(1H, s), 11.88(1H, s).

10 **Example 103**

Ethyl 4,7-dihydro-4-(indan-4-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from indan-4-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner

15 as in Example 1.

MP:181-183°C.

Anal. Calcd. for: C₂₁H₂₅N₃O₂: C, 71.77; H, 7.17; N, 11.96.

Found: C, 71.66; H, 7.14; N, 11.88.

MS(EI): 351(M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90(3H, t, J=7.3Hz), 0.90(3H, t, J=7.3Hz), 1.62(2H, m), 1.80-2.10(2H, m), 2.52-3.10(6H, m), 3.77(2H, q, J=7.3Hz), 5.17(1H, s), 6.81(1H, d, J=6.8Hz), 6.91-6.96(2H, m), 7.14(1H, s), 9.33(1H, br.s), 11.87(1H, br.s).

25 **Example 104**

Ethyl 4,7-dihydro-6-propyl-4-(1,2,3,4-tetrahydronaphthalen-5-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Example 105

Ethyl 4-(benzo[b]furan-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30

Example 106

Ethyl 4-(benzo[b]thiophen-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from benzo[b]thiophene-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:166°C.

5 Anal. Calcd. for: $C_{20}H_{21}N_3O_2S \cdot 2H_2O$: C, 59.53; H, 6.25; N, 10.41.

Found: C, 59.77; H, 6.46; N, 9.95.

MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.74(3, t, $J=7.3$ Hz),
0.97(3H, t, $J=7.3$ Hz), 1.65-1.69(2H, m), 2.70-2.80(2H, m),
10 3.71(2H, q, $J=7.3$ Hz), 5.48(1H, s), 7.11-7.13(2H, m),
7.26(1H, dd, $J=7.4$ Hz and 7.5Hz), 7.39(1H, d, $J=5.4$ Hz),
7.63(1H, d, $J=7.3$ Hz), 7.68(1H, d, $J=5.4$ Hz), 9.57(1H, s),
11.91(1H, s).

Example 107

15 5'-Ethoxycarbonyl-4',7'-dihydro-6'-propyl-
spiro[benzo[b]thiophene-3(2H),4'-2'H-pyrazolo[3,4-b]pyridine]

To a solution of 5'-ethoxycarbonyl-4',7'-dihydro-6'-propyl-spiro[benzo[b]thiophene-3(2H), 4'-2'H-pyrazolo[3,4-b]pyridine]-1-oxide (100 mg) in carbon tetrachloride (20 mL)
20 was added trimethylsilane iodide (0.1 g), and the mixture was stirred with heating for 30 minutes. The reaction mixture was allowed to cool to ambient temperature, and the mixture was extracted with chloroform. The solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified
25 by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (20 mg) as colorless crystals.

MP:147°C.

Anal. Calcd. for: $C_{19}H_{21}N_3O_2S$: C, 64.20; H, 5.95; N, 11.82.

30 Found: C, 64.18; H, 6.14; N, 11.56.

MS(EI): 355 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.73(3H, t, $J=7.3$ Hz),
0.95(3H, t, $J=7.3$ Hz), 1.64-1.67(2H, m), 2.56-2.64(2H, m),

3.03(1H,d,J=10.2Hz), 3.72(2H,q,J=7.3Hz), 4.03(1H,d,J=10.2Hz),
6.69(1H,d,J=7.3Hz), 6.91(1H,dd,J=7.3Hz and 7.4Hz),
7.03(1H,dd,J=7.3Hz and 7.4Hz), 7.08(1H,s), 7.15(1H,d,J=7.3Hz),
9.65(1H,br.s), 11.96(1H,br.s).

5 **Example 108**

Ethyl 4,7-dihydro-4-methyl-4-phenyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 5'-ethoxycarbonyl-4',7'-dihydro-6'-propyl-spiro[benzo[b]thiophene-3(2H), 4'-2'H-pyrazolo[3,4-b]pyridin]-1-oxide (100 mg) in tetrahydrofuran (10 mL) were
10 added disodium hydrogenphosphate (1.2 g) and methanol (5 mL) under ice-cooling, and 10% sodium amalgam (3.0 g) was added. The mixture was stirred for 5 hours, filtered through Celite and extracted with chloroform. The solvent was evaporated
15 under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (80 mg) as colorless crystals.

MP:207°C.

20 Anal. Calcd. for: C₁₉H₂₃N₃O₂: C, 70.13; H, 7.12; N, 12.91.

Found: C, 69.89; H, 7.18; N, 12.99.

MS(EI): 325(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.71(3H,t,J=7.3Hz),
0.96(3H,t,J=7.3Hz), 1.64-1.68(2H,m), 2.28(3H,s), 2.48-
25 2.56(2H,m), 3.71(2H,q,J=7.3Hz), 6.73-7.01(5H,m), 7.10(1H,s),
9.71(1H,br.s), 11.87(1H,br.s).

Example 109

Ethyl 4,7-dihydro-6-propyl-4-(2,3,5-trichlorophenyl)-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 2,3,5-trichlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:218-220°C (decomposition).

Anal. Calcd. for: $C_{18}H_{18}Cl_3N_3O_2$: C, 52.13; H, 4.37; N, 10.13.

Found: C, 51.76; H, 4.37; N, 10.07.

MS(EI): 414 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=6.9Hz),
5 0.97(3H, t, J=7.3Hz), 1.62-1.67(2H, m), 2.65-2.71(1H, m), 2.85-
2.92(1H, m), 3.76-3.88(2H, m), 5.62(1H, s), 7.03(1H, d, J=1.6Hz),
7.33(1H, s), 7.59(1H, d, J=2.4Hz), 9.69(1H, s), 12.12(1H, s).

Example 110

Ethyl 4,7-dihydro-6-propyl-4-(2,3,4,5-
10 tetrahydrobenzo[b]oxepin-9-yl)-2H-pyrazolo[3,4-b]pyridine-5-
carboxylate

Example 111

Ethyl 4-(3-chloro-2-methylphenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from 3-chloro-2-
methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
in the same manner as in Example 1.

MP: 185°C.

Anal. Calcd. for: $C_{19}H_{22}ClN_3O_2$: C, 63.42; H, 6.16; N, 11.68.

20 Found: C, 63.37; H, 6.12; N, 11.65.

MS(EI): 359 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87(3H, t, J=7.3Hz),
0.95(3H, t, J=7.3Hz), 1.60-1.66(2H, m), 2.67-2.69(1H, m), 2.74-
2.78(1H, m), 3.78(2H, q, J=7.3Hz), 5.39(1H, s), 6.95(1H, d, J=7.3Hz),
25 7.04(1H, dd, J=7.3Hz and 7.4Hz), 7.12(1H, d, J=7.3Hz), 7.24(1H, s),
9.44(1H, br.s), 11.94(1H, br.s).

Example 112

Ethyl 4-(2,1,3-benzothiadiazol-4-yl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 2,1,3-
benzothiadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-
ketohexanoate in the same manner as in Example 25.

MP: 180°C.

Anal. Calcd. for: $C_{18}H_{19}N_5O_2S$: C, 58.52; H, 5.18; N, 18.96.

Found: C, 58.51; H, 5.19; N, 18.81.

MS(EI): 369 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.62(3H, t, $J=7.3$ Hz),
5 1.00(3H, t, $J=7.3$ Hz), 1.68-1.72(2H, m), 2.76-2.89(2H, m),
3.72(2H, q, $J=7.3$ Hz), 6.02(1H, s), 7.16(1H, s), 7.20(1H, d, $J=7.3$ Hz),
7.60(1H, dd, $J=7.3$ Hz and 7.4Hz), 7.83(1H, d, $J=7.3$ Hz), 9.55(1H, s),
11.89(1H, s).

Example 113

10 Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl acetoacetate in the same manner as in Example 25.

15 MP: 228°C.

Anal. Calcd. for: $C_{16}H_{15}N_5O_3$: C, 59.07; H, 4.65; N, 21.53.

Found: C, 58.85; H, 4.75; N, 21.17.

MS(EI): 325 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.75(3H, t, $J=7.3$ Hz), 2.42(3H, s),
20 3.79(2H, q, $J=7.3$ Hz), 5.67(1H, s), 7.14(1H, d, $J=6.6$ Hz),
7.23(1H, s), 7.49(1H, dd, $J=9.0$ Hz and 6.6Hz), 7.78(1H, d, $J=9.0$ Hz),
9.69(1H, s), 12.02(1H, s).

Example 114

25 Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl benzoylacetate in the same manner as in Example 1.

MP: 190°C.

30 Anal. Calcd. for: $C_{21}H_{17}N_5O_3$: C, 65.11; H, 4.42; N, 18.08.

Found: C, 64.99; H, 4.59; N, 18.06.

MS(EI): 387 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.54(3H, t, $J=7.3$ Hz),

3.56(2H,q,J=7.3Hz), 5.68(1H,s), 7.24(1H,s), 7.26-7.42(6H,m),
7.72(1H,dd,J=7.3Hz and 7.2Hz), 7.94(1H,d,J=7.3Hz),
9.71(1H,s),12.08(1H,s).

Example 115

5 Ethyl 4-(2,3-dichlorophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-dichlorobenzaldehyde, 3-aminopyrazole and ethyl benzoylacetate in the same manner as in Example 1.

10 MP:214°C.

Anal. Calcd. for: C₂₁H₁₇N₅O₃: C, 65.11; H, 4.42; N, 18.08.

Found: C, 64.85; H, 4.48; N, 17.92.

MS(EI): 387(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.57(3H,t,J=7.3Hz),

15 3.52(2H,q,J=7.3Hz), 5.70(1H,s), 7.30-7.40(9H,m), 9.61(1H,s),
12.12(1H,s).

Example 116

(+)Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The compound described in Example 76 was separated using a semi-preparative column for optical resolution (CHIRALPAK AS, 1.0 cm×25 cm, eluent n-hexane/2-propanol/diethylamine=90/10/0.1, flow rate 2.0 mL/min, UV 254 nm, retention time 40 minutes, DAICEL CHEMICAL INDUSTRIES,
25 LTD.) to give the title compound as colorless crystals.

MP: 159°C.

MS(EI): 353(M⁺).

Specific rotation: [α]_D=+260°(EtOH,c=0.5).

Example 117

30 (-)Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The compound described in Example 76 was separated using a semi-preparative column for optical resolution (CHIRALPAK AS,

1.0 cm×25 cm, eluent n-hexane/2-propanol/diethylamine=90/10/0.1, flow rate 2.0 mL/min, UV 254 nm, retention time 55 minutes, DAICEL CHEMICAL INDUSTRIES, LTD.) to give the title compound as colorless crystals.

5 MP: 160°C.

MS(EI): 353(M⁺).

Specific rotation: $[\alpha]_D = -277^\circ$ (EtOH, c=0.5).

Example 118

4-(2-Bromophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP: 226°C.

15 Anal. Calcd. for: C₁₅H₁₅BrN₄O₂: C, 49.60; H, 4.16; N, 15.43.

Found: C, 49.57; H, 4.28; N, 14.96.

MS(EI): 363(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.02(3H, t, J=7.3Hz), 1.72-1.76(2H, m), 2.85-3.05(2H, m), 5.89(1H, s), 7.07-7.1(2H, m),
20 7.25(1H, dd, J=7.5Hz and 7.4Hz), 7.47(1H, s), 7.56(1H, d, J=7.3Hz), 10.84(1H, s), 12.43(1H, s).

Example 119

4,7-Dihydro-4-(2-methoxyphenyl)-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from n-butylaldehyde, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP: 223°C.

Anal. Calcd. for: C₁₆H₁₈N₄O₃: C, 61.13; H, 5.77; N, 17.82.

30 Found: C, 61.01; H, 5.87; N, 17.92.

MS(EI): 314(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.03(3H, t, J=7.3Hz), 1.72-1.78(2H, m), 2.82-3.04(2H, m), 3.86(3H, s), 5.76(1H, s),

6.78(1H,dd,J=7.5Hz and 7.4Hz), 6.90(1H,d,J=7.3Hz),
6.95(1H,d,J=7.3Hz), 7.10(1H,dd,J=7.5Hz and 7.4Hz), 7.33(1H,s),
10.68(1H,s), 12.29(1H,s).

Example 120

5 4,7-Dihydro-4-(2-methylthiophenyl)-5-nitro-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

10 MP:211°C.

Anal. Calcd. for: C₁₆H₁₈N₄O₂S: C, 58.16; H, 5.49; N, 16.96.

Found: C, 57.94; H, 5.47; N, 16.53.

MS(EI): 330(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.02(3H,t,J=7.3z), 1.71-
15 1.76(2H,m), 2.8-3.00(2H,m), 5.89(1H,s), 6.98(1H,d,J=7.3Hz),
7.03(1H,dd,J=7.5Hz and 7.4Hz), 7.13(1H,dd,J=7.5Hz and 7.4Hz),
7.28(1H,d,J=7.3Hz), 7.41(1H,s), 10.74(1H,s), 12.34(1H,s).

Example 121

20 4,7-Dihydro-5-nitro-4-(2-nitrophenyl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP:204°C.

25 Anal. Calcd. for: C₁₅H₁₅N₅O₄: C, 54.71; H, 4.59; N, 21.27.

Found: C, 54.50; H, 4.77; N, 21.32.

MS(EI): 329(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.01(3H,t,J=7.3Hz), 1.69-
1.74(2H,m), 2.85-2.99(2H,m), 5.67(1H,s), 6.94(1H,d,J=7.3Hz),
30 6.98-7.03(2H,m), 7.09(1H,d,J=7.3Hz), 7.38(1H,s), 10.69(1H,s),
12.34(1H,s).

Example 122

4-(2,3-Dichlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-

pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

5 MP:239°C.

Anal. Calcd. for: $C_{15}H_{14}Cl_2N_4O_2$: C, 51.01; H, 4.00; N, 15.86.

Found: C, 50.70; H, 4.06; N, 15.60.

MS(EI): 353(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.02(3H, t, J=7.3Hz), 1.70-
10 1.74(2H, m), 2.89-2.92(1H, m), 2.96-3.02(1H, m), 5.96(1H, s),
7.09(1H, d, J=7.3Hz), 7.24(1H, dd, J=7.5Hz and 7.4Hz),
7.43(1H, d, J=7.3Hz), 7.49(1H, s), 10.98(1H, s), 12.49(1H, s).

Example 1234,7-Dihydro-4-(naphthalen-1-yl)-5-nitro-6-propyl-2H-

15 pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, naphthalen-1-aldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP:226°C.

20 Anal. Calcd. for: $C_{19}H_{16}N_4O_2$: C, 68.25; H, 5.43; N, 16.76.

Found: C, 68.29; H, 5.20; N, 16.67.

MS(EI): 334(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.06(3H, t, J=7.3Hz), 1.76-
1.82(2H, m), 2.95-3.06(2H, m), 6.33(1H, s), 7.18-7.22(2H, m),
25 7.36(1H, dd, J=7.5Hz and 7.4Hz), 7.54(1H, dd, J=7.5Hz and 7.4Hz),
7.60(1H, dd, J=7.5Hz and 7.4Hz), 7.71(1H, d, J=7.3Hz),
7.92(1H, d, J=7.3Hz), 8.46(1H, d, J=7.3Hz), 10.80(1H, s),
12.29(1H, s).

Example 124

30 4,7-Dihydro-4-(3,4-dihydro-2H-benzopyran-8-yl)-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 3,4-dihydro-2H-benzopyran-8-aldehyde and 3-aminopyrazole in

the same manner as in Example 93.

MP:234°C.

Anal. Calcd. for: $C_{18}H_{20}N_4O_3$: C, 63.52; H, 5.92; N, 16.46.

Found: C, 63.22; H, 5.94; N, 16.44.

5 MS(EI): 340(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.02(3H, t, $J=7.3$ Hz), 1.71-1.77(2H, m), 1.92-1.95(2H, m), 2.69-2.73(2H, m), 2.85-3.02(2H, m), 4.23-4.28(2, m), 5.71(1H, s), 6.61-6.67(2H, m), 6.80(1H, d, $J=7.3$ Hz), 7.37(1H, s), 10.64(1H, s), 12.28(1H, s).

10 **Example 125**

4-(2,3-Dichlorophenyl)-4,7-dihydro-6-methyl-5-nitro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from acetaldehyde, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as
15 in Example 93.

MP:>270°C.

Anal. Calcd. for: $C_{13}H_{10}Cl_2N_4O_2$: C, 48.02; H, 3.10; N, 17.23.

Found: C, 48.05; H, 3.12; N, 17.24.

MS(EI): 325(M^+).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.66(3H, s), 5.94(1H, s), 7.13(1H, d, $J=7.2$ Hz), 7.22(1H, dd, $J=7.3$ Hz and 7.2Hz), 7.42(1H, d, $J=7.3$ Hz), 7.50(1H, s), 10.94(1H, s), 12.49(1H, s).

Example 126

4-(2,3-Dichlorophenyl)-6-ethyl-4,7-dihydro-5-nitro-2H-pyrazolo[3,4-b]pyridine
25

The title compound was prepared from propionaldehyde, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP:250°C.

30 Anal. Calcd. for: $C_{14}H_{12}Cl_2N_4O_2$: C, 49.58; H, 3.57; N, 16.52.

Found: C, 49.54; H, 3.62; N, 16.73.

MS(EI): 339(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.29(3H, t, $J=7.3$ Hz), 2.98-

3.01(2H,m), 5.94(1H,s), 7.10(1H,d,J=7.3Hz), 7.24(1H,dd,J=7.3Hz and 7.2Hz), 7.42(1H,d,J=7.2Hz), 7.49(1H,s), 10.93(1H,s), 12.49(1H,s).

Example 127

5 6-Butyl-4-(2,3-dichlorophenyl)-4,7-dihydro-5-nitro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from pentylaldehyde, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

10 MP:220°C.

Anal. Calcd. for: C₁₆H₁₆Cl₂N₄O₂: C, 52.33; H, 4.39; N, 15.26.

Found: C, 52.64; H, 4.61; N, 14.51.

MS(EI): 367(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H,t,J=7.3Hz), 1.41-
15 1.46(2H,m), 1.63-1.68(2H,m), 2.94-3.04(2H,m), 5.95(1H,s),
7.08(1H,d,J=7.2Hz), 7.23(1H,dd,J=7.3Hz and 7.2Hz),
7.42(1H,d,J=7.2Hz), 7.48(1H,s), 10.97(1H,s), 12.28(1H,s).

Example 128

20 4-(2-Bromophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:237°C.

25 Anal. Calcd. for: C₁₆H₁₅BrN₄: C, 55.99; H, 4.41; N, 16.32.

Found: C, 55.97; H, 4.45; N, 16.40.

MS(EI): 343(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.95(3H,t,J=7.3Hz), 1.64-
1.70(2,m), 2.40-2.44(2H,m), 5.35(1H,s), 7.15(1H,dd,J=7.5Hz and
30 7.4Hz), 7.22(1H,d,J=7.3Hz), 7.27(1H,s), 7.36(1H,dd,J=7.5Hz and
7.4Hz), 7.59(1H,d,J=7.3Hz), 9.84(1H,s), 12.16(1H,s).

Example 129

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-

pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

5 MP:203°C.

Anal. Calcd. for: C₁₇H₁₆N₄O: C, 69.37; H, 6.16; N, 19.03.

Found: C, 69.34; H, 6.25; N, 19.01.

MS(EI): 294(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.96(3H, t, J=7.3Hz), 1.65-
10 1.70(2H, m), 2.38-2.43(2H, m), 3.83(3H, s), 5.22(1H, s),
6.89(1H, dd, J=7.5Hz and 7.4Hz), 6.99(1H, d, J=7.3Hz),
7.05(1H, d, J=7.3Hz), 7.15-7.18(2H, m), 9.65(1H, s), 12.02(1H, s).

Example 1305-Cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-propyl-2H-

15 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:216°C.

20 Anal. Calcd. for: C₁₇H₁₆N₄S: C, 65.78; H, 5.84; N, 18.05.

Found: C, 65.68; H, 5.81; N, 17.83.

MS(EI): 310(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.96(3H, t, J=7.3Hz), 1.65-
1.70(2H, m), 2.40-2.46(2H, m), 2.48(3H, s), 5.34(1H, s), 7.13-
25 7.21(4H, m), 7.30(1H, d, J=7.3Hz), 9.75(1H, s), 12.07(1H, s).

Example 1315-Cyano-4,7-dihydro-4-(2-methylphenyl)-6-propyl-2H-pyrazolo
[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
30 2-methylbenzaldehyde and 3-aminopyrazole in the same manner as
in Example 94.

MP:230°C.

Anal. Calcd. for: C₁₇H₁₆N₄: C, 73.35; H, 6.52; N, 20.13.

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PCT/JP02/00829

12.22(1H,s).

Example 134

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl butanoate, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:242°C.

Anal. Calcd. for: C₁₆H₁₄Cl₂N₄ 1/5 H₂O: C, 57.05; H, 4.31; N, 16.63.

10 Found: C, 57.23; H, 4.49; N, 16.25.

MS(EI): 333(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.62-1.68(2H, m), 2.40-2.46(2H, m), 5.44(1H, s), 7.22(1H, d, J=7.3Hz), 7.30(1H, s), 7.35(1H, dd, J=7.5Hz and 7.4Hz), 7.51(1H, d, J=7.3Hz),
15 9.89(1H, s), 12.19(1H, s).

Example 135

5-Cyano-4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl butanoate, naphthalene-1-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:263°C.

Anal. Calcd. for: C₂₀H₁₈N₄: C, 76.41; H, 5.77; N, 17.82.

Found: C, 76.05; H, 5.85; N, 17.73.

25 MS(EI): 314(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.97(3H, t, J=7.3Hz), 1.68-1.73(2H, m), 2.44-2.48(2H, m), 5.71(1H, s), 7.04(1H, s), 7.39-7.46(4H, m), 7.81(1H, d, J=7.3Hz), 7.94(1H, d, J=7.3Hz), 9.83(1H, s),
12.02(1H, s).

30 **Example 136**

5-Cyano-4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,

3,4-dihydro-2H-benzopyran-8-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:230°C.

Anal. Calcd. for: $C_{19}H_{20}N_4O$: C, 71.23; H, 6.29; N, 17.49.

5 Found: C, 71.20; H, 6.48; N, 17.55.

MS(EI): 320 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, J=7.3Hz), 1.64-1.70(2H, m), 1.92-1.95(2H, m), 2.38-2.43(2H, m), 2.72-2.76(2H, m), 4.16-4.27(2H, m), 5.16(1H, s), 6.74(1H, dd, J=7.5Hz and 7.4Hz),
10 6.83-6.88(2H, m), 7.20(1H, s), 9.62(1H, s), 12.01(1H, s).

Example 137

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
15 2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:194°C.

Anal. Calcd. for: $C_{16}H_{14}N_6O$: C, 62.73; H, 4.61; N, 27.44.

Found: C, 62.52; H, 4.78; N, 27.19.

20 MS(EI): 306 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, J=7.3Hz), 1.63-1.68(2H, m), 2.38-2.43(2H, m), 5.40(1H, s), 7.25(1H, s), 7.40(1H, d, J=7.3Hz), 7.58(1H, dd, J=7.5Hz and 7.4Hz), 7.92(1H, d, J=7.3z), 9.93(1H, s), 12.13(1H, s).

25 Example 138

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
2,1,3-benzothiadiazol-4-aldehyde and 3-aminopyrazole in the
30 same manner as in Example 94.

MP:195°C.

Anal. Calcd. for: $C_{16}H_{14}N_6S$: C, 59.61; H, 4.38; N, 26.07.

Found: C, 59.33; H, 4.48; N, 25.76.

MS(EI): 322(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.98(3H, t, J=7.3Hz), 1.68-
1.74(2H, m), 2.45-2.50(2H, m), 5.72(1H, s), 7.19(1H, s),
7.43(1H, d, J=7.3Hz), 7.72(1H, dd, J=7.5Hz and 7.4Hz),
5 7.97(1H, d, J=7.3Hz), 9.87(1H, s), 12.06(1H, s).

Example 139

5-Cyano-4,7-dihydro-4-(2-methylbenzoxazol-4-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
10 2-methylbenzoxazole-4-aldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: 208°C.

Anal. Calcd. for: C₁₈H₁₇N₅O 1/5 H₂O: C, 66.94; H, 5.43; N, 21.68.

Found: C, 66.85; H, 5.52; N, 22.09.

15 MS(EI): 319(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.97(3H, t, J=7.3Hz), 1.67-
1.72(2H, m), 2.40-2.45(2H, m), 2.63(3H, s), 5.51(1H, s),
7.06(1H, d, J=7.3Hz), 7.16(1H, s), 7.29(1H, dd, J=7.3Hz and 7.2Hz),
7.47(1H, d, J=7.3Hz), 9.77(1H, s), 12.06(1H, s).

20 **Example 140**

R(-) 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

To a solution of the compound described in Example 137
(64.5 g) in THF (1000 mL) was added (-)camphorsulfonic acid
25 (49 g) at room temperature and the mixture was stirred for 1
hour. The solvent was evaporated under reduced pressure to
give an oil. The obtained oil was recrystallized from
acetonitrile twice to give colorless crystals (11 g). To a
solution of the obtained colorless crystals in methanol (50
30 mL) was added water (50 mL). The mixture was neutralized with
a saturated aqueous sodium hydrogencarbonate solution and
extracted with ethyl acetate. The solvent was evaporated under
reduced pressure. The residual methanol solution was added

dropwise to water (1000 mL) and the crystals were collected by filtration to give the title compound (11 g) as pale-yellow crystals.

(CHIRALPAK AS, 0.25 cm×25 cm, eluent n-hexane/2-

5 propanol/diethylamine =80/20/0.1, flow rate 1.5 mL/min, UV 254 nm, retention time 10 minutes, DAICEL CHEMICAL INDUSTRIES, LTD.)

MP: 170°C.

MS(EI): 306(M⁺).

10 Specific rotation: [α]_D=-80°(EtOH,c=1.0).

Example 141

S(+) 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

To a solution of the compound (54 g), which was
15 recovered from the mother liquor obtained in Example 140, in THF (600 mL) was added (+)camphorsulfonic acid (41 g) at room temperature and the mixture was stirred for 1 hour. The solvent was evaporated under reduced pressure to give an oil. The obtained oil was recrystallized from acetonitrile twice to
20 give colorless crystals (12 g). To a solution of the obtained colorless crystals in methanol (50 mL) was added water (50 mL). The mixture was neutralized with a saturated aqueous sodium hydrogencarbonate solution and extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the
25 residual methanol solution was added dropwise to water (1000 mL). The crystals were collected by filtration to give the title compound (11 g) as pale-yellow crystals.

(CHIRALPAK AS, 0.25 cm×25 cm, eluent n-hexane/2-

propanol/diethylamine =80/20/0.1, flow rate 1.5 mL/min, UV 254
30 nm, retention time 13 minutes, DAICEL CHEMICAL INDUSTRIES, LTD.)

MP: 170°C.

MS(EI): 306(M⁺).

Specific rotation: $[\alpha]_D^{25} = +82^\circ$ (EtOH, $c = 1.0$).

Example 142

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl benzoate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 158°C.

Anal. Calcd. for: $C_{19}H_{13}ClN_4$ H_2O : C, 65.05; H, 4.31; N, 15.97.

10 Found: C, 65.35; H, 4.19; N, 16.21.

MS(EI): 332 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.51(1H, s), 7.25-7.51(8H, m), 7.59-7.61(2H, m), 10.07(1H, s), 12.24(1H, s).

Example 143

15 5-Cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

20 MP: 146°C.

Anal. Calcd. for: $C_{20}H_{16}N_4S$ $4/5 H_2O$: C, 66.94; H, 4.94; N, 15.61.

Found: C, 66.85; H, 4.81; N, 15.65.

MS(EI): 344 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.48(3H, s), 5.48(1H, s), 7.19-7.33(5H, m), 7.48-7.50(3H, m), 7.59-7.61(2H, m), 9.99(1H, s), 12.16(1H, s).

Example 144

5-Cyano-4-(2-cyanophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl benzoate, 2-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 148°C.

Anal. Calcd. for: $C_{20}H_{13}N_5 \cdot 3/5 H_2O$: C, 71.89; H, 4.28; N, 20.96.

Found: C, 71.89; H, 4.33; N, 20.91.

MS(EI): 323 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.38(1H, s), 7.31(1H, s), 7.44-
5 7.59(7H, m), 7.70(1H, dd, J=7.3Hz and 7.2Hz), 7.83(1H, d, J=7.3Hz),
10.21(1H, s), 12.31(1H, s).

Example 145

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-phenyl-2H-
pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl benzoate,
2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 95.

MP: 162°C.

Anal. Calcd. for: $C_{19}H_{12}Cl_2N_4$: C, 62.14; H, 3.29; N, 15.26.

15 Found: C, 61.57; H, 3.93; N, 17.19.

MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.59(1H, s), 7.37-7.42(3H, m),
7.48-7.55(4H, m), 7.59-7.62(2H, m), 10.14(1H, s), 12.28(1H, s).

Example 146

20 5-Cyano-4,7-dihydro-4-(naphthalen-1-yl)-6-phenyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate,
naphthalene-1-benzaldehyde and 3-aminopyrazole in the same
manner as in Example 95.

25 MP: 174°C.

Anal. Calcd. for: $C_{23}H_{16}N_4$: C, 79.29; H, 4.63; N, 16.08.

Found: C, 79.50; H, 4.85; N, 16.58.

MS(EI): 348 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.87(1H, s), 7.12(1H, s), 7.50-
30 7.63(9H, m), 7.82(1H, d, J=7.3Hz), 7.96(1H, d, J=7.3Hz),
8.34(1H, d, J=7.3Hz), 10.09(1H, s), 12.12(1H, s).

Example 147

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-

pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

5 MP:>270°C.

Anal. Calcd. for: C₂₀H₁₂BrN₅: C, 59.72; H, 3.01; N, 17.41.

Found: C, 59.53; H, 3.17; N, 17.30.

MS(EI): 402(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.63(1H, s), 7.39(1H, s), 7.49-
10 7.51(3H, m), 7.60-7.63(3H, m), 7.75(1H, d, J=7.3Hz),
7.85(1H, d, J=7.3Hz), 10.21(1H, s), 12.33(1H, s).

Example 1485-Cyano-4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from methyl benzoate, 3,4-dihydro-2H-benzopyran-8-benzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 255°C.

Anal. Calcd. for: C₂₂H₁₆N₄O: C, 74.56; H, 5.12; N, 15.81.

20 Found: C, 74.27; H, 5.11; N, 15.82.

MS(EI): 354(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.94-1.97(2H, m), 2.75-2.78(2H, m),
4.20-4.30(2H, m), 5.30(1H, s), 6.80(1H, dd, J=7.3Hz and 7.2Hz),
6.91(1H, d, J=7.3Hz), 7.02(1H, d, J=7.3Hz), 7.28(1H, s), 7.49-
25 7.51(3H, m), 7.60-7.63(2H, m), 9.88(1H, s), 12.11(1H, s).

Example 1495-Cyano-4-(2,3-difluorophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate,
30 2,3-difluorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 165°C.

Anal. Calcd. for: C₁₉H₁₂F₂N₄ 3/5 H₂O: C, 66.12; H, 3.86; N, 16.23.

Found: C, 65.87; H, 3.81; N, 16.46.

MS(EI): 334(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.40(1H, s), 7.16-7.38(4H, m), 7.48-7.50(3H, m), 7.57-7.59(2H, m), 10.11(1H, s), 12.30(1H, s).

5 **Example 150**

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as
10 in Example 95.

MP: 206°C.

Anal. Calcd. for: C₂₀H₁₆N₄O: C, 73.15; H, 4.91; N, 17.06.

Found: C, 73.23; H, 5.14; N, 17.19.

MS(EI): 328(M⁺).

15 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.86(3H, s), 5.36(1H, s), 6.94(1H, dd, J=7.3Hz and 7.2Hz), 7.02(1H, d, J=7.3Hz), 7.19-7.25(3H, m), 7.48-7.51(3H, m), 7.60-7.63(2H, m), 9.91(1H, s), 12.12(1H, s).

Example 151

20 5-Cyano-4,7-dihydro-4,6-bis(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl o-anisate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

25 MP: 220°C.

Anal. Calcd. for: C₂₁H₁₈N₄O₂: C, 70.38; H, 5.06; N, 15.63.

Found: C, 69.97; H, 5.13; N, 16.15.

MS(EI): 358(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.86(3H, s), 3.88(3H, s),
30 5.32(1H, s), 6.95-7.06(3H, m), 7.14-7.25(3H, m), 7.37(1H, d, J=7.3Hz), 7.45(1H, dd, J=7.3Hz and 7.2Hz), 9.74(1H, s), 12.05(1H, s).

Example 152

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(3-methoxyphenyl)-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl m-anisate,
2-methoxybenzaldehyde and 3-aminopyrazole in the same manner
5 as in Example 95.

MP:192°C.

Anal. Calcd. for: $C_{21}H_{18}N_4O_2$: C, 70.38; H, 5.06; N, 15.63.

Found: C, 69.97; H, 5.09; N, 15.54.

MS(EI): 358(M^+).

10 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.81(3H, s), 3.86(3H, s),
5.35(1H, s), 6.95(1H, dd, J=7.3Hz and 7.2Hz), 7.01(1H, d, J=7.3Hz),
7.07(1H, d, J=7.3Hz), 7.14(1H, s), 7.18-7.23(5H, m),
7.41(1H, dd, J=7.3Hz and 7.2Hz), 9.88(1H, s), 12.12(1H, s).

Example 153

15 5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(4-methoxyphenyl)-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl p-anisate,
2-methoxybenzaldehyde and 3-aminopyrazole in the same manner
as in Example 95.

20 MP:149°C.

Anal. Calcd. for: $C_{21}H_{18}N_4O_2 \cdot 1/2 H_2O$: C, 68.65; H, 5.21; N, 15.25.

Found: C, 68.67; H, 4.99; N, 15.35.

MS(EI): 358(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.81(3H, s), 3.86(3H, s),
25 5.33(1H, s), 6.94(1H, dd, J=7.3Hz and 7.2Hz), 7.01-7.05(3H, m),
7.18-7.24(3H, m), 7.56(2H, d, J=7.2Hz), 9.82(1H, s), 12.10(1H, s).

Example 154

5-Cyano-4,7-dihydro-4-(2-nitrophenyl)-6-phenyl-2H-
pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl benzoate, 2-
nitrobenzaldehyde and 3-aminopyrazole in the same manner as in
Example 95.

MP:221°C.

Anal. Calcd. for: $C_{19}H_{13}N_5O_2$: C, 66.47; H, 3.82; N, 20.40.

Found: C, 66.48; H, 4.08; N, 20.41.

MS(EI): 343(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54(1H, s), 7.34(1H, s), 7.49-
5 7.52(4H, m), 7.59-7.64(3H, m), 7.74(1H, dd, $J=7.3$ Hz and 7.2Hz),
7.91(1H, d, $J=7.3$ Hz), 10.16(1H, s), 12.30(1H, s).

Example 155

5-Cyano-4,7-dihydro-6-(2-methoxyphenyl)-4-(2-nitrophenyl)-2H-
pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl o-anisate,
2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as
in Example 95.

MP: 207°C.

Anal. Calcd. for: $C_{20}H_{15}N_5O_3$: C, 64.34; H, 4.05; N, 18.76.

15 Found: C, 64.03; H, 4.21; N, 18.68.

MS(EI): 373(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.85(3H, s), 5.50(1H, s),
7.03(1H, dd, $J=7.3$ Hz and 7.2Hz), 7.14(1H, d, $J=7.3$ Hz), 7.33(1H, s),
7.37(1H, d, $J=7.3$ Hz), 7.44-7.52(2H, m), 7.74-7.80(2H, m),
20 7.92(1H, d, $J=7.3$ Hz), 10.02(1H, s), 12.25(1H, s).

Example 156

5-Cyano-4,7-dihydro-6-(3-methoxyphenyl)-4-(2-nitrophenyl)-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl m-anisate,
25 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as
in Example 95.

MP: 220°C.

Anal. Calcd. for: $C_{20}H_{15}N_5O_3$: C, 64.34; H, 4.05; N, 18.76.

Found: C, 63.92; H, 4.14; N, 18.74.

30 MS(EI): 373(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.81(3H, s), 5.53(1H, s),
7.07(1H, d, $J=7.3$ Hz), 7.14-7.18(2H, m), 7.33(1H, s),
7.40(1H, dd, $J=7.3$ Hz and 7.2Hz), 7.50(1H, dd, $J=7.3$ Hz and 7.2Hz),

7.63(1H,d,J=7.3Hz), 7.74(1H,dd,J=7.3Hz 7.2Hz),
7.91(1H,d,J=7.3Hz), 10.13(1H,s), 12.30(1H,s).

Example 157

5-Cyano-4,7-dihydro-6-(4-methoxyphenyl)-4-(2-nitrophenyl)-2H-
5 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl p-anisate,
2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as
in Example 95.

MP:215°C.

10 Anal. Calcd. for: C₂₀H₁₅N₅O₃: C, 64.34; H, 4.05; N, 18.76.

Found: C, 64.13; H, 4.12; N, 18.69.

MS(EI): 373(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 3.81(3H,s), 5.51(1H,s),
7.03(2H,d,J=7.3Hz), 7.33(1H,s), 7.47-7.55(3H,m), 7.61(1H,d),
15 7.74(1H,dd,J=7.3Hz and 7.2Hz), 7.91(1H,d,J=7.3Hz), 10.07(1H,s),
12.28(1H,s).

Example 158

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-2H-
pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl benzoate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:231°C.

Anal. Calcd. for: C₁₉H₁₂N₆O: C, 67.05; H, 3.55; N, 24.69.

25 Found: C, 66.76; H, 3.90; N, 24.71.

MS(EI): 340(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 5.55(1H,s), 7.33(1H,s), 7.50-
7.64(7H,m), 7.95(1H,d,J=7.3Hz), 10.20(1H,s), 12.23(1H,s).

Example 159

30 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-
methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl o-anisate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the

same manner as in Example 95.

MP:180°C.

Anal. Calcd. for: C₂₀H₁₄N₆O₂: C, 64.86; H, 3.81; N, 22.69.

Found: C, 64.11; H, 3.98; N, 22.34.

5 MS(EI): 370(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.84(3H, s), 5.56(1H, s),
7.03(1H, dd, J=7.3Hz and 7.2Hz), 7.14(1H, d, J=6.8Hz), 7.33-
7.35(2H, m), 7.45(1H, dd, J=7.3Hz and 7.2Hz), 7.54(1H, d, J=7.3Hz),
7.65(1H, dd, J=8.8Hz and 6.8Hz), 7.94(1H, d, J=8.8Hz), 10.04(1H, s),
10 12.18(1H, s).

Example 160

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(3-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl m-anisate,
15 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:198°C.

Anal. Calcd. for: C₂₀H₁₄N₆O₂ 4/5 H₂O: C, 62.43; H, 4.09; N, 21.84.

Found: C, 62.60; H, 3.99; N, 22.15.

20 MS(EI): 370(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.80(3H, s), 5.55(1H, s), 7.06-
7.17(3H, m), 7.33(1H, s), 7.40(1H, dd, J=7.3Hz),
7.52(1H, d, J=6.6Hz), 7.62(1H, dd, J=8.8Hz and 6.8Hz),
7.95(1H, d, J=6.8Hz), 10.18(1H, s), 12.24(1H, s).

25 Example 161

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl p-anisate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
30 same manner as in Example 95.

MP:244°C.

Anal. Calcd. for: C₂₀H₁₄N₆O₂: C, 64.86; H, 3.81; N, 22.69.

Found: C, 64.77; H, 3.91; N, 22.49.

MS(EI):370(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 3.80(3H,s), 5.53(1H,s),
7.02(2H,d,J=7.3Hz), 7.32(1H,s), 7.50-7.53(3H,m),
7.61(1H,dd,J=8.8Hz and 6.8Hz), 7.94(1H,d,J=8.8Hz), 10.11(1H,s),
5 12.21(1H,s).

Example 162

4-(2,1,3-Benzothiadiaazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate,
10 2,1,3-benzothiadiaazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:258°C.

MS(EI):356(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 5.85(1H,s), 7.27(1H,s), 7.51-
15 7.52(3H,m), 7.61-7.67(3H,m), 7.76(1H,dd,J=8.8Hz and 6.8Hz),
8.00(1H,d,J=8.8Hz), 10.13(1H,s), 12.16(1H,s).

Example 163

4-(2,1,3-Benzothiadiaazol-4-yl)-5-cyano-4,7-dihydro-6-(2-
methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl o-anisate,
2,1,3-benzothiadiaazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:231°C.

Anal. Calcd. for:C₂₀H₁₄N₆OS 3/10 H₂O:C,61.30;H,3.76;N,21.45.

25 Found:C,61.24;H,3.74;N,22.09.

MS(EI):386(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 3.89(3H,s),5.85(1H,s),
7.06(1H,dd,J=7.6Hz and 7.3Hz), 7.17(1H,d,J=8.3Hz), 7.28(1H,s),
7.43-7.49(2H,m), 7.69(1H,d,J=6.8Hz), 7.80(1H,dd,J=8.8Hz and
30 6.8Hz), 7.99(1H,d,J=8.8Hz), 9.97(1H,s), 12.11(1H,s).

Example 164

4-(2,1,3-Benzothiadiaazol-4-yl)-5-cyano-4,7-dihydro-6-(3-
methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl m-anisate, 2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:220°C.

5 Anal. Calcd. for: C₂₀H₁₄N₆OS: C, 62.16; H, 3.65; N, 21.75.

Found: C, 61.98; H, 3.70; N, 21.66.

MS(EI): 386 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.82(3H, s), 5.85(1H, s),
7.08(1H, d, J=8.3Hz), 7.19(1H, s), 7.23-7.27(2H, m),
10 7.42(1H, dd, J=7.8Hz and 7.2Hz), 7.61(1H, d, J=6.6Hz),
7.75(1H, dd, J=8.8Hz and 6.8Hz), 7.99(1H, d, J=8.1Hz), 10.10(1H, s),
12.16(1H, s).

Example 165

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-
15 methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl p-anisate, 2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:238°C.

20 MS(EI): 386 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.81(3H, s), 5.83(1H, s),
7.04(2H, d, J=8.8Hz), 7.26(1H, s), 7.73-7.77(3H, m),
7.75(1H, dd, J=8.8Hz and 6.8Hz), 7.99(1H, d, J=8.8Hz), 10.04(1H, s),
12.14(1H, s).

25 Example 166

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(pyridin-4-
yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isonicotinate, 2,1,3-benzoxadiazole-4-aldehyde and 3-
30 aminopyrazole in the same manner as in Example 95.

MP:236°C.

MS(EI): 341 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.58(1H, s), 7.35(1H, s), 7.54-

7.64(4H,m), 7.96(1H,d,J=8.1Hz), 8.72(2H,d,J=5.9Hz),
10.40(1H,s), 12.29(1H,s).

Example 167

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-pyridin-
5 3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl nicotinate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:216°C.

10 Anal. Calcd. for: C₁₈H₁₁N₇O 1/5 H₂O: C, 62.68; H, 3.33; N, 28.43.

Found: C, 62.73; H, 3.43; N, 28.30.

MS(EI): 341(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.59(1H,s), 7.35(1H,s), 7.52-
7.63(3H,m), 7.95-8.00(2H,m), 8.69(1H,d,J=4.9Hz), 8.76(1H,s),
15 10.39(1H,s), 12.28(1H,s).

Example 168

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-pyridin-
2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl picolinate,
20 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:188°C.

MS(EI): 341(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.59(1H,s), 7.34(1H,s), 7.51-
25 7.53(2H,m), 7.63(1H,dd,J=9.0Hz and 6.6Hz), 7.75(1H,d,J=6.6Hz),
7.95-7.97(2H,m), 8.69(1H,d,J=5.4Hz), 10.20(1H,s), 12.26(1H,s).

Example 169

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-
(naphthalen-1-yl)-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl 1-naphthoate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:213°C.

Anal. Calcd. for: $C_{23}H_{14}N_6O$: C, 70.76; H, 3.61; N, 21.53.

Found: C, 70.33; H, 3.74; N, 21.23.

MS(EI): 390 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.65(1H, s), 7.35-7.66(7H, m),
5 7.96-8.21(4H, m), 10.35(1H, s), 12.23(1H, s).

Example 170

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(furan-2-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl furan-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 241°C.

Anal. Calcd. for: $C_{17}H_{10}N_6O_2$: C, 61.82; H, 3.05; N, 25.44.

Found: C, 61.72; H, 3.19; N, 25.34.

15 MS(EI): 330 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54(1H, s), 6.69(1H, s),
7.22(1H, d, J=3.4Hz), 7.32(1H, s), 7.48(1H, d, J=6.3Hz),
7.61(1H, dd, J=9.0Hz and 6.3Hz), 7.89(1H, s), 7.94(1H, d, J=9.0Hz),
10.17(1H, s), 12.26(1H, s).

20 Example 171

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 230°C.

Anal. Calcd. for: $C_{17}H_{10}N_6OS$: C, 58.95; H, 2.91; N, 24.26.

Found: C, 58.71; H, 3.08; N, 24.03.

MS(EI): 346 (M^+).

30 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54(1H, s), 7.17(1H, dd, J=4.9Hz and 4.8Hz), 7.33(1H, s), 7.49(1H, d, J=6.6Hz), 7.58-7.64(2H, m),
7.77(1H, d, J=4.9Hz), 7.95(1H, d, J=9.0Hz), 10.21(1H, s),
12.27(1H, s).

Example 172

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(naphthalen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 2-naphthoate,
5 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:228°C.

Anal. Calcd. for: C₂₃H₁₄N₆O: C, 70.76; H, 3.61; N, 21.53.

Found: C, 70.66; H, 3.81; N, 20.94.

10 MS(EI): 390(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.48(1H, s), 7.24(1H, s), 7.44-
7.55(5H, m), 7.85-7.92(4H, m), 8.05(1H, s), 10.21(1H, s),
12.14(1H, s).

Example 173

15 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(furan-2-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl furan-3-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

20 MP:237°C.

Anal. Calcd. for: C₁₇H₁₀N₆O₂: C, 61.82; H, 3.05; N, 25.44.

Found: C, 61.59; H, 3.27; N, 25.01.

MS(EI): 330(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.52(1H, s), 6.93(1H, d, J=1.0Hz),
25 7.31(1H, s), 7.48(1H, d, J=6.6Hz), 7.60(1H, dd, J=9.0Hz and 6.6Hz),
7.80(1H, dd, J=1.0Hz), 7.94(1H, d, J=9.0Hz), 8.24(1H, s),
10.07(1H, s), 12.25(1H, s).

Example 174

30 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-3-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:242°C.

Anal. Calcd. for: C₁₇H₁₀N₆OS: C, 58.95; H, 2.91; N, 24.26.

Found: C, 58.52; H, 3.15; N, 23.92.

MS(EI): 346(M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.54(1H, s), 7.32(1H, s),
7.42(1H, d, J=5.1Hz), 7.50(1H, d, J=6.6Hz), 7.61-7.66(2H, m),
7.94(1H, d, J=9.0Hz), 8.00(1H, s), 10.13(1H, s), 12.24(1H, s).

Example 175

6-(Benzo[b]furan-2-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-
10 4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzo[b]furan-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:>270°C.

15 Anal. Calcd. for: C₂₁H₁₂N₆O₂: C, 66.31; H, 3.18; N, 22.09.

Found: C, 66.26; H, 3.34; N, 21.53.

MS(EI): 380(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.62(1H, s), 7.31-7.36(2H, m),
7.45(1H, dd, J=9.0Hz and 6.7Hz), 7.53(1H, d, J=6.7Hz), 7.61-
20 7.65(3H, m), 7.77(1H, d, J=7.3Hz), 7.96(1H, d, J=9.0Hz),
10.44(1H, s), 12.33(1H, s).

Example 176

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-methyl-2H-
pyrazolo[3,4-b]pyridine

25 The title compound was prepared from ethyl acetate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:212°C.

Anal. Calcd. for: C₁₄H₁₀N₆O 3/5 H₂O: C, 58.17; H, 3.91; N, 29.07.

30 Found: C, 58.45; H, 4.08; N, 28.61.

MS(EI): 278(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.14(3H, s), 5.40(1H, s),
7.25(1H, s), 7.40(1H, d, J=6.6Hz), 7.59(1H, dd, J=9.0Hz 6.6Hz),

7.92(1H,d,J=9.0Hz), 9.98(1H,s), 12.13(1H,s).

Example 177

4-(2,1,3-Benzoxadiazol-4-yl)-6-butyl-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl pentanoate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:200°C.

Anal. Calcd. for: C₁₇H₁₆N₆O: C, 63.74; H, 5.03; N, 26.23.

10 Found: C, 63.85; H, 5.01; N, 26.26.

MS(EI): 320 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H,t,J=7.3Hz), 1.30-1.39(2H,m), 1.57-1.65(2H,m), 2.06-2.40(2H,m), 5.39(1H,s), 7.25(1H,s), 7.39(1H,d,J=6.6Hz), 7.59(1H,dd,J=9.0Hz and 6.6Hz),
15 7.91(1H,d,J=9.0Hz), 9.94(1H,s), 12.13(1H,s).

Example 178

Ethyl 4-(2-chloro-3-methylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

A suspension of 2-chloro-m-xylene (15 ml), N-
20 bromosuccinimide (23.3 g) and benzoyl peroxide (200 mg) in carbon tetrachloride (150 ml) was heated under reflux for 6 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography
25 (eluent: hexane) to give 2-bromomethyl-1-chloro-6-methylbenzene (16.0 g) as a colorless oil. 2-Bromomethyl-1-chloro-6-methylbenzene (25.4 g) and hexamethylenetetramine (32.4 g) were dissolved in acetic acid-water (1:1, 10 ml) and the mixture was heated under reflux for 5 hours. To the
30 reaction mixture was added concentrated hydrochloric acid (40 ml) and the mixture was heated under reflux for 1 hour. The reaction mixture was extracted with ethyl acetate. The extract was washed with an aqueous sodium hydrogencarbonate solution

and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give 2-chloro-3-methylbenzaldehyde (19.4 g) as a yellow oil. Subsequently, the title compound was prepared from 2-chloro-3-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:198-200°C.

Anal. Calcd. for: $C_{19}H_{22}ClN_3O_2$: C, 63.42; H, 6.16; N, 11.68.

Found: C, 63.19; H, 6.14; N, 11.71.

10 MS(EI): 359 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.85(3H, t, $J=7.3$ Hz), 0.97(3H, t, $J=7.3$ Hz), 1.65(2H, m), 2.33(3H, s), 2.68-2.71(1H, m), 2.79-2.84(1H, m), 3.72-3.82(2H, m), 5.63(1H, s), 6.93-6.96(1H, m), 7.05-7.07(2H, m), 7.24(1H, s), 9.46(1H, s), 11.94(1H, s).

15 **Example 179**

Ethyl 4-(2-chloro-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 2-chloro-3-nitrobenzoic acid (5.0 g) in THF (50 ml) was added borane-tetrahydrofuran complex (1M THF solution, 30 ml) under ice-cooling and the mixture was stirred at room temperature for 24 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract was washed with water and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give a pale-yellow solid (3.7 g). The obtained pale-yellow solid (1.6 g) and manganese dioxide (1.7 g) were heated under reflux in toluene for 4.5 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (4:1)) to give 2-chloro-3-nitrobenzaldehyde (1.3 g) as a pale-yellow solid. Subsequently, the title compound

was prepared from 2-chloro-3-nitrobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MS(EI): 390(M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=6.8Hz), 0.97(3H, t, J=7.3Hz), 1.64-1.68(2H, m), 2.70-2.85(2H, m), 3.73-3.86(2H, m), 5.67(1H, s), 7.31(1H, s), 7.39-7.47(2H, m), 7.73(1H, dd, J=1.5, 7.8Hz), 9.67(1H, s), 12.10(1H, s).

Example 180

10 Ethyl 4-(2-chloro-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 2-chloro-3-methylbenzaldehyde (19.4 g) in ethanol (45 ml) was added an aqueous hydroxylamine hydrochloride (9.7 g) solution (12 ml), and an aqueous sodium
15 hydroxide (6.9 g) solution (10-ml) was added. The mixture was stirred at room temperature for 1.5 hours. Water (500 ml) was added and the precipitated crystals were collected by filtration. The obtained white crystals (16.1 g) were dissolved in acetic anhydride (50 ml) and the mixture was
20 heated under reflux for 2.5 hours. The reaction mixture was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (5:1)) to give 2-cyano-6-methylchlorobenzene (10.9 g) as a white solid. A suspension of
25 2-cyano-6-methylchlorobenzene (10.9 g), N-bromosuccinimide (12.8 g) and benzoyl peroxide (523 mg) in carbon tetrachloride (100 ml) was heated under reflux for 3.5 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by
30 silica gel column chromatography (eluent: hexane-ethyl acetate (20:1)) to give 2-chloro-3-cyanobenzaldehyde (12.8 g) as a colorless oil. Subsequently, the title compound was prepared from 2-chloro-3-cyanobenzaldehyde, 3-aminopyrazole and ethyl

3-ketohexanoate in the same manner as in Example 25.

MP: 213–215°C.

Anal. Calcd. for: C₁₉H₁₉ClN₄O₂: C, 61.54; H, 5.16; N, 15.11.

Found: C, 61.25; H, 5.36; N, 14.71.

5 MS(EI): 370(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.86(3H, t, J=6.9Hz),
0.96(3H, t, J=7.3Hz), 1.65(2H, m), 2.70–2.80(2H, m), 3.73–
3.81(2H, m), 5.63(1H, s), 7.31(1H, s), 7.42–7.44(2H, m),
7.72(1H, dd, J=3.0, 6.4Hz), 9.65(1H, s), 12.08(1H, s).

10 IR(KBr): ν=3344, 3292, 2985, 2954, 2242, 1652 cm⁻¹.

Example 181

Ethyl 4-(2,3-dibromophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

A suspension of 2-bromo-3-nitrotoluene (5.0 g), iron
15 (3.9 g) and ammonium chloride (3.7 g) in ethanol (50 ml)-water
(17 ml) was heated under reflux for 2 hours. The insoluble
matter was filtered off. To the filtrate was added ethyl
acetate (100 ml) and the mixture was washed with water and a
saturated aqueous sodium chloride solution, and dried over
20 anhydrous magnesium sulfate. The solvent was evaporated and
the obtained residue was purified by silica gel column
chromatography (eluent: hexane-ethyl acetate (5:1)) to give a
pale-yellow oil (4.8 g). The obtained pale-yellow oil (4.8 g)
was dissolved in 47% hydrobromic acid (50 ml). Under ice-
25 cooling, an aqueous sodium nitrite (1.6 g) solution (18 ml)
was added and the mixture was stirred under ice-cooling for 30
minutes. The reaction mixture was added dropwise to a solution
of cuprous bromide (2.0 g) in 47% hydrobromic acid (20 ml)
over 30 minutes and the mixture was stirred at 60°C for 4.5
30 hours. To the reaction mixture was added water (100 ml) and
the mixture was extracted with ethyl acetate. The extract was
washed with water and a saturated aqueous sodium
hydrogencarbonate solution, and dried over anhydrous magnesium

sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (9:1)) to give 2,3-dibromotoluene (2.6 g) as a brown oil. A suspension of 2,3-dibromotoluene (2.6 g), N-bromosuccinimide (1.85 g) and benzoyl peroxide (50 mg) in carbon tetrachloride (30 ml) was heated under reflux for 2 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane) to give a colorless oil (1.1 g). To a solution of the obtained colorless oil (1.1 g) in dimethyl sulfoxide (8.6 ml) - methylene chloride (2 ml) was added trimethylamine-N-oxide (1.0 g) under ice-cooling and the mixture was stirred at room temperature for 1 hour. The reaction mixture was poured into water (50 ml) and the mixture was extracted with ethyl acetate. The extract was washed with 5% hydrochloric acid, a saturated aqueous sodium hydrogencarbonate solution and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give 2,3-dibromobenzaldehyde (0.5 g) as a brown oil. Then the title compound was prepared from 2,3-dibromobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:180-183°C (decomposition).

MS(EI):469(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.86(3H, t, J=7.3Hz), 0.96(3H, t, J=7.3Hz), 1.65(2H, m), 2.70-2.80(2H, m), 3.72-3.83(2H, m), 5.67(1H, s), 7.07(1H, d, J=5.8Hz), 7.18(1H, dd, J=5.8, 7.8Hz), 7.48(1H, d, J=7.8Hz), 9.57(1H, s), 12.02(1H, s).

IR(KBr):ν=3344, 3292, 2985, 2954, 2242, 1652cm⁻¹.

Example 182

Ethyl 4-(2-bromo-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate 1/2 H₂O

A suspension of 2-bromo-3-nitrotoluene (5.1 g), N-bromosuccinimide (4.2 g) and benzoyl peroxide (229 mg) in carbon tetrachloride (50 ml) was heated under reflux for 3
5 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give a yellow solid (5.4 g). The obtained yellow solid (5.4 g) and
10 hexamethylenetetramine (5.1 g) were dissolved in acetic acid-water (1:1, 16 ml) and the mixture was heated under reflux for 2 hours. To the reaction mixture was added concentrated hydrochloric acid (6 ml) and the mixture was heated under reflux for 15 minutes. The reaction mixture was extracted with
15 ethyl acetate. The extract was washed with water, an aqueous sodium hydrogencarbonate solution and a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the obtained residue was purified by silica gel column chromatography (eluent:
20 hexane-ethyl acetate (5:1)) and crystallized (hexane-ethyl acetate (5:1)) to give 2-bromo-3-nitrobenzaldehyde (1.2 g) as yellow crystals. Subsequently, the title compound was prepared from 2-bromo-3-nitrobenzaldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 25.

25 MP:213-215°C.

Anal. Calcd. for: C₁₈H₁₉BrN₄O₄ 1/2 H₂O: C, 48.66; H, 4.54; N, 12.61.

Found: C, 48.34; H, 4.20; N, 13.04.

MS(EI): 435(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.3Hz),
30 0.97(3H, t, J=7.3Hz), 1.63-1.68(2H, m), 2.77-2.81(2H, m), 3.72-3.85(2H, m), 5.68(1H, s), 7.33-7.36(2H, m),
7.47(1H, dd, J=7.8, 7.8Hz), 7.66(1H, d, J=7.8Hz), 9.67(1H, s),
12.09(1H, s).

Example 183

Ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-bromo-m-xylene,
5 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner
as in Example 180.

MP:210-212°C (decomposition).

Anal. Calcd. for: C₁₉H₁₉BrN₄O₂: C, 54.95; H, 4.61; N, 13.49.

Found: C, 54.98; H, 4.94; N, 13.11.

10 MS(EI): 415(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=6.8Hz),
0.97(3H, t, J=7.3Hz), 1.62-1.68(2H, m), 2.75-2.80(2H, m), 3.72-
3.83(2H, m), 5.63(1H, s), 7.32(1H, s), 7.39-7.48(2H, m),
7.68(1H, dd, J=1.9, 7.3Hz), 9.65(1H, s), 12.07(1H, s).

15 **Example 184**

4-(2-Chloro-3-cyanophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
2-chloro-3-cyanobenzaldehyde and 3-aminopyrazole in the same
20 manner as in Example 94.

MP: >250°C.

Anal. Calcd. for: C₁₇H₁₄Cl₃N₅: C, 63.06; H, 4.36; N, 21.63.

Found: C, 63.10; H, 4.42; N, 21.61.

MS(EI): 323(M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.61-
1.71(2H, m), 2.35-2.49(2H, m), 5.47(1H, s), 7.32(1H, s), 7.52-
7.59(2H, m), 7.87(1H, dd, J=2.0, 7.3Hz), 9.95(1H, s), 12.24(1H, s).

Example 185

4-(2-Chloro-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
2-chloro-3-nitrobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:234-235°C.

Anal. Calcd. for: $C_{16}H_{14}ClN_5O_2$: C, 55.90; H, 4.10; N, 20.37.

Found: C, 55.93; H, 4.34; N, 20.72.

MS(EI): 343 (M^+).

5 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94(3H, t, J=7.3Hz), 1.64-1.69(2H, m), 2.37-2.45(2H, m), 5.52(1H, s), 7.34(1H, s), 7.54-7.60(2H, m), 7.89(1H, dd, J=2.0, 6.9Hz), 9.97(1H, s), 12.25(1H, s).

Example 186

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-
10 pyrazolo[3,4-b]pyridine 1/5 H₂O

The title compound was prepared from methyl butanoate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:275-279°C (decomposition).

15 Anal. Calcd. for: $C_{17}H_{14}BrN_5$ 1/5 H₂O: C, 55.05; H, 3.89; N, 18.88.

Found: C, 54.98; H, 3.91; N, 18.81.

MS(EI): 368 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94(3H, t, J=7.3Hz), 1.64-1.69(2H, m), 2.38-2.43(2H, m), 5.47(1H, s), 7.33(1H, s), 7.54-
20 7.60(2H, m), 7.83(1H, dd, J=2.0, 7.4Hz), 9.95(1H, s), 12.24(1H, s).

Example 187

(+)Ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-
propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of the compound (1.94 g) described in
25 Example 73 in acetonitrile (15 ml) was added (-)-10-camphorsulfonic acid (1.23 g) at 50°C and the mixture was stirred under ice-cooling for 30 minutes. The precipitated crystals were collected by filtration and recrystallized (ethanol-ethyl acetate (2:1), 30 ml) to give white crystals
30 (0.81 g). The obtained white crystals were suspended in water and a saturated aqueous sodium hydrogencarbonate solution was added. The mixture was extracted with ethyl acetate and the extract was washed with water and a saturated aqueous sodium

chloride solution, and dried over anhydrous magnesium sulfate.
The solvent was evaporated to give a colorless transparent oil.
The obtained colorless transparent oil was crystallized from
ethyl acetate to give the title compound (470 mg) as white
5 crystals.

MP:159-161°C.

Anal. Calcd. for: $C_{21}H_{25}N_3O_3$: C, 68.64; H, 6.86; N, 11.44.

Found: C, 68.37; H, 6.86; N, 11.26.

Specific rotation: $[\alpha]_D^{20} = +200^\circ$ (EtOH, c=0.5).

10 MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, J=6.8Hz),
0.98(3H, t, J=7.3Hz), 1.60-1.70(2H, m), 1.90-2.00(2H, m), 2.67-
2.82(4H, m), 3.81(2H, m), 4.25(2H, m), 5.42(1H, s),
6.62(1H, dd, J=7.4, 7.8Hz), 6.72-6.76(2H, m), 7.18(1H, s),
15 9.26(1H, s), 11.81(1H, s).

Example 188

(-)-Ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-
propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The filtrate obtained by filtering off the (-)-10-
20 camphorsulfonate salt in Example 187 was concentrated under
reduced pressure and suspended in water. To the suspension was
added a saturated aqueous sodium hydrogencarbonate solution
and the mixture was extracted with ethyl acetate. The extract
was washed with a saturated aqueous sodium chloride solution
25 and dried over anhydrous magnesium sulfate. The solvent was
evaporated and the obtained residue was crystallized from
ethyl acetate to give white crystals (780 mg). By the same
process as in Example 187 using the obtained white crystals
and (+)-10-camphorsulfonic acid, the title compound (150 mg)
30 was obtained as white crystals.

MP:160-161°C.

Anal. Calcd. for: $C_{21}H_{25}N_3O_3$: C, 68.64; H, 6.86; N, 11.44.

Found: C, 68.49; H, 6.81; N, 11.42.

Specific rotation: $[\alpha]_D = -202^\circ$ (EtOH, $c=0.5$)

MS(EI): 367 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, $J=6.8\text{Hz}$),
0.98(3H, t, $J=7.3\text{Hz}$), 1.60-1.70(2H, m), 1.90-2.00(2H, m), 2.67-
5 2.82(4H, m), 3.81(2H, m), 4.25(2H, m), 5.42(1H, s), 6.62(1H, dd,
 $J=7.4, 7.8\text{Hz}$), 6.72-6.76(2H, m), 7.18(1H, s), 9.26(1H, s),
11.81(1H, s).

Example 189

4-(2-Bromo-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-
10 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-bromo-3-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 250-255°C (decomposition).

15 Anal. Calcd. for: $\text{C}_{16}\text{H}_{14}\text{BrN}_5\text{O}_2$: C, 49.50; H, 3.63; N, 18.04.

Found: C, 49.37; H, 3.76; N, 18.02.

MS(EI): 388 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, $J=7.6\text{Hz}$), 1.64-
1.70(2H, m), 2.39-2.44(2H, m), 5.53(1H, s), 7.34(1H, s),
20 7.49(1H, d, $J=7.8\text{Hz}$), 7.60(1H, dd, $J=7.8, 8.0\text{Hz}$),
7.82(1H, d, $J=8.0\text{Hz}$), 9.97(1H, s), 12.25(1H, s).

Example 190

Ethyl 4,7-dihydro-4-(2-methoxy-3-methylphenyl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

25 A suspension of 2,6-dimethylphenol (19.5 g), iodomethane (31 ml) and potassium carbonate (33.2 g) in dimethylformamide (200 ml) was stirred at 60°C for 10 hours. The reaction mixture was poured into water (300 ml) and the mixture was extracted with ethyl acetate. The extract was washed with a
30 saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane) to give 2-methoxy-m-xylene (12

g) as a colorless oil. A suspension of 2-methoxy-m-xylene (5.1 g), N-bromosuccinimide (4.2 g) and benzoyl peroxide (229 mg) in carbon tetrachloride (50 ml) was heated under reflux for 3 hours. The insoluble material was filtered off and the
5 filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give a yellow solid (5.4 g). The obtained yellow solid (5.4 g) and hexamethylenetetramine (5.1 g) were dissolved in acetic acid-
10 water (1:1, 16 ml) and the mixture was heated under reflux for 2 hours. To the reaction mixture was added concentrated hydrochloric acid (6 ml) and the mixture was heated under reflux for 15 minutes. The reaction mixture was extracted with ethyl acetate. The extract was washed with water, an aqueous
15 sodium hydrogencarbonate solution and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (5:1)) and crystallized (hexane-ethyl
20 acetate (5:1)) to give 2-methoxy-3-methylbenzaldehyde (1.2 g) as yellow crystals. Subsequently, the title compound was prepared from 2-methoxy-3-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25. MP: 220-222°C.

25 Anal. Calcd. for: $C_{20}H_{25}N_3O_3$: C, 67.58; H, 7.09; N, 11.82.

Found: C, 67.47; H, 7.02; N, 11.91.

MS(EI): 355 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=7.0Hz),
0.97(3H, t, J=7.3Hz), 1.60-1.70(2H, m), 2.23(3H, s), 2.66-
30 2.85(2H, m), 3.81(3H, s), 3.81-3.85(2H, m), 5.43(1H, s), 6.82-
6.91(3H, m), 7.13(1H, s), 9.31(1H, s), 11.82(1H, s).

Example 191

Ethyl 4-(3-cyano-2-methoxyphenyl)-4,7-dihydro-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxy-3-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 180.

5 MP:220-222°C.

Anal. Calcd. for: C₂₀H₂₂N₄O₃: C, 65.56; H, 6.05; N, 15.29.

Found: C, 65.20; H, 6.10; N, 15.23.

MS(EI): 366(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H, t, J=7.1Hz),
10 0.96(3H, t, J=7.3Hz), 1.60-1.70(2H, m), 2.70-2.80(2H, m), 3.75-
3.90(2H, m), 4.02(3H, s), 5.46(1H, s), 7.14-7.19(2H, m),
7.32(1H, d, J=6.1Hz), 7.53(1H, d, J=7.8Hz), 9.51(1H, s),
11.97(1H, s).

Example 192

15 5-Cyano-6-ethyl-4,7-dihydro-4-(2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

20 MP:228-230°C (decomposition).

Anal. Calcd. for: C₁₅H₁₃N₅O₂: C, 61.01; H, 4.44; N, 23.72.

Found: C, 60.72; H, 4.51; N, 23.78.

MS(EI): 295(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, t, J=7.4Hz), 2.42-
25 2.49(2H, m), 5.37(1H, s), 7.27(1H, s), 7.43-7.49(2H, m),
7.70(1H, dd, J=7.6, 8.0Hz), 7.89(1H, d, J=8.0Hz), 9.94(1H, s),
12.21(1H, s).

Example 193

5-Cyano-4-(2,3-dichlorophenyl)-6-ethyl-4,7-dihydro-2H-
30 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 2,3-dichlorobenzaldehyde, 3-aminopyrazole and 1-cyanobutan-2-one in the same manner as in Example 94.

MP:>300°C.

Anal. Calcd. for: C₁₅H₁₂Cl₂N₄: C, 56.44; H, 3.79; N, 17.55.

Found: C, 56.33; H, 3.86; N, 17.67.

MS(EI): 319(M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, t, J=7.6Hz), 2.38-
2.49(2H, m), 5.43(1H, s), 7.23(1H, d, J=6.8Hz), 7.31-7.37(2H, m),
7.51(1H, dd, J=1.7, 8.1Hz), 9.92(1H, s), 12.19(1H, s).

Example 194

5-Cyano-6-ethyl-4,7-dihydro-4-(2-methoxyphenyl)-2H-

10 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 230-232°C.

15 Anal. Calcd. for: C₁₆H₁₆N₄O: C, 68.55; H, 5.75; N, 19.99.

Found: C, 68.16; H, 5.97; N, 20.39.

MS(EI): 280(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.22(3H, t, J=7.6Hz), 2.42-
2.49(2H, m), 3.84(3H, s), 5.21(1H, s), 6.86-6.91(1H, m),
20 6.99(1H, d, J=8.3Hz), 7.05(1H, d, J=7.6Hz), 7.15-7.19(2H, m),
9.68(1H, s), 12.02(1H, s).

Example 195

4-(2-Chloro-3-cyanophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl propionate, 2-chloro-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>300°C.

Anal. Calcd. for: C₁₆H₁₂ClN₅: C, 62.04; H, 3.90; N, 22.61.

30 Found: C, 61.74; H, 4.14; N, 22.93.

MS(EI): 309(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, t, J=7.6Hz), 2.42-
2.49(2H, m), 5.45(1H, s), 7.33(1H, s), 7.52-7.60(2H, m), 7.87

(1H,dd,J=2.0,7.3Hz), 9.97(1H,s), 12.23(1H,s).

Example 196

4-(2,1,3-Benzoxazol-4-yl)-5-cyano-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl propionate, 2,1,3-benzoxazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:206-208°C (decomposition).

Anal. Calcd. for: C₁₅H₁₂N₆O: C, 61.64; H, 4.14; N, 28.75.

10 Found: C, 61.43; H, 4.41; N, 28.85.

MS(EI): 292(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.20(3H,t,J=7.6Hz), 2.40-2.50(2H,m), 5.40(1H,s), 7.26(1H,s), 7.40(1H,d,J=6.6Hz), 7.58(1H,dd,J=6.6,9.0Hz), 7.92(1H,d,J=9.0Hz), 9.97(1H,s),
15 12.14(1H,s).

Example 197

4-(2-Chlorophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl propionate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>300°C.

Anal. Calcd. for: C₁₅H₁₃ClN₄: C, 63.27; H, 4.60; N, 19.68.

Found: C, 63.14; H, 4.69; N, 19.67.

25 MS(EI): 284(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H,t,J=7.6Hz), 2.42-2.49(2H,m), 5.35(1H,s), 7.22-7.26(3H,m), 7.30-7.34(1H,m), 7.42(1H,d,J=7.8Hz), 9.85(1H,s), 12.15(1H,s).

Example 198

30 4-(2-Bromo-3-cyanophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

 The title compound was prepared from methyl propionate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same

manner as in Example 94.

MP:>300°C.

Anal. Calcd. for: C₁₆H₁₂BrN₅: C, 54.25; H, 3.41; N, 19.77.

Found: C, 54.13; H, 3.56; N, 19.98.

5 MS(EI): 354(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, t, J=7.6Hz), 2.43(2H, m),
5.46(1H, s), 7.33(1H, s), 7.56-7.60(2H, m), 7.82-7.84(1H, m),
9.98(1H, s), 12.24(1H, s).

Example 199

10 4-(2-Bromophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-
b]pyridine

The title compound was prepared from methyl propionate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

15 MP: 250-253°C (decomposition).

Anal. Calcd. for: C₁₅H₁₃BrN₄: C, 54.73; H, 3.98; N, 17.02.

Found: C, 54.28; H, 3.96; N, 16.94.

MS(EI): 329(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, t, J=7.6Hz), 2.42-
20 2.45(2H, m), 5.34(1H, s), 7.16(1H, dd, J=7.5, 7.6Hz),
7.22(1H, d, J=6.6Hz), 7.27(1H, s), 7.36(1H, dd, J=6.3, 7.3Hz),
7.59(1H, d, J=6.8Hz), 9.86(1H, s), 12.15(1H, s).

Example 200

Ethyl 4-(2-chlorophenyl)-6-cyano-4,7-dihydro-2H-pyrazolo[3,4-
25 b]pyridine-5-carboxylate 1/4 hydrate

A solution of 1,1'-carbonylbis-1H-imidazole (22.5 g), ethanol (8.1 ml) and toluene (100 ml) was stirred at room temperature for 1.5 hours. To the reaction mixture was added ice-water (100 ml) and the mixture was extracted with ethyl
30 acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent:

hexane-ethyl acetate (1:1)) to give a colorless oil (19.3 g).
A solution of the obtained residue (19.3 g) and pyruvic
aldehyde dimethyl acetal (11.1 ml) in toluene (50 ml) was
added dropwise to a suspension of sodium hydride (8.44 g) in
5 toluene (250 ml) under reflux with heating over 15 minutes,
and the mixture was heated under reflux for 1.5 hours. To the
reaction mixture was added a 10% aqueous citric acid solution
(610 ml) and the mixture was extracted with ethyl acetate. The
extract was washed with a saturated aqueous sodium chloride
10 solution and dried over anhydrous magnesium sulfate. The
solvent was evaporated and the obtained residue was purified
by silica gel column chromatography (eluent: hexane-ethyl
acetate (5:1)) to give ethyl 4,4-dimethoxy-3-oxobutanoate
(15.1 g) as a colorless oil. Subsequently, ethyl 4-(2-
15 chlorophenyl)-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate was obtained as a yellow solid from
2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 4,4-dimethoxy-
2-oxobutanoate in the same manner as in Example 1. To a
solution of ethyl 4-(2-chlorophenyl)-6-dimethoxymethyl-4,7-
20 dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (463 mg) in
tetrahydrofuran (5 ml) was added 1N hydrochloric acid (10 ml)
and the mixture was stirred at room temperature for 6 hours.
To the reaction mixture was added a saturated aqueous sodium
hydrogencarbonate solution and the mixture was extracted with
25 ethyl acetate. The extract was washed with a saturated aqueous
sodium chloride solution and dried over anhydrous magnesium
sulfate. The solvent was evaporated and the obtained residue
was purified by silica gel column chromatography (eluent:
hexane-ethyl acetate (1:1)) to give ethyl 4-(2-chlorophenyl)-
30 6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate
(290 mg) as a yellow solid. A solution of ethyl 4-(2-
chlorophenyl)-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-
5-carboxylate (290 mg) and hydroxylamine-O-sulfonic acid

(128.5 mg) in water (10 ml)-ethanol (10 ml) was stirred at 80°C for 2 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) and crystallized from ethanol-ethyl acetate to give the title compound (53 mg) as yellow crystals.

MP: 275-278°C (decomposition).

Anal. Calcd. for: $C_{16}H_{13}ClN_4O_2 \cdot \frac{1}{4} H_2O$: C, 57.66; H, 4.08; N, 16.81.

Found: C, 57.54; H, 4.06; N, 16.66.

MS(EI): 328 (M^+).

1H -NMR (400 MHz, DMSO- d_6) δ (ppm): 0.93 (3H, t, $J=7.1$ Hz), 3.91 (2H, m), 5.67 (1H, s), 7.15-7.19 (2H, m), 7.25 (1H, dd, $J=7.3, 8.3$ Hz), 7.33 (1H, s), 7.39 (1H, d, $J=8.3$ Hz), 10.81 (1H, s), 12.34 (1H, s).

Example 201

4-(2-Chloro-3-trifluoromethylphenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-chloro-3-trifluoromethylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: >250°C.

Anal. Calcd. for: $C_{17}H_{14}ClF_3N_4$: C, 55.67; H, 3.85; N, 15.28.

Found: C, 55.81; H, 3.97; N, 15.44.

MS(EI): 366 (M^+).

1H -NMR (400 MHz, DMSO- d_6) δ (ppm): 0.95 (3H, t, $J=7.3$ Hz), 1.64-1.70 (2H, m), 2.40-2.43 (2H, m), 5.55 (1H, s), 7.31 (1H, s), 7.54-7.56 (2H, m), 7.74 (1H, dd, $J=3.6, 5.6$ Hz), 9.93 (1H, s), 12.22 (1H, s).

Example 202

4-(2-Chloro-3-trifluoromethylphenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from benzoic acid, 2-chloro-3-trifluoromethylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:>250°C.

5 Anal. Calcd. for: C₂₀H₁₂ClF₃N₄: C, 59.94; H, 3.02; N, 13.98.

Found: C, 59.74; H, 3.18; N, 13.95.

MS(EI): 400(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 5.70(1H, s), 7.39(1H, s), 7.49-7.51(3H, m), 7.57-7.62(3H, m), 7.75-7.79(2H, m), 10.18(1H, s),
10 12.31(1H, s).

Example 203

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
15 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₆H₁₅ClN₄: C, 64.32; H, 5.06; N, 18.75.

Found: C, 64.18; H, 5.12; N, 18.84.

20 MS(EI): 298(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.23(3H, d, J=6.8Hz), 1.27(3H, d, J=6.8Hz), 3.06(1H, m), 5.34(1H, s), 7.22-7.26(3H, m), 7.30-7.34(1H, m), 7.42(1H, d, J=7.1Hz), 9.63(1H, s), 12.16(1H, s).

Example 204

25 Ethyl 1-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of the compound (1.2 g) described in Example 27 and dimethylaminopyridine (128 mg) in THF (40 ml) was added di-tert-butylidicarbonate (830 mg) and the mixture
30 was stirred at room temperature for one day. The solvent was evaporated under reduced pressure and the title compound (102 mg) was obtained as colorless crystals by silica gel column chromatography (eluent: hexane-ethyl acetate (3:1)).

MP:112-116°C.

Anal. Calcd. for: $C_{23}H_{28}ClN_3O_4$: C, 61.95; H, 6.33; N, 9.42.

Found: C, 61.84; H, 6.33; N, 9.34.

MS(EI): 445 (M^+).

5 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87(3H, t, J=6.9Hz),
0.98(3H, t, J=7.3Hz), 1.56(9H, s), 1.62-1.72(2H, m), 2.80-
2.92(2H, m), 3.85(2H, q, J=6.9Hz), 5.56(1H, s), 7.14-7.17(2H, m),
7.23(1H, dd, J=7.3 and 7.8Hz), 7.30(1H, s), 7.39(1H, d, J=7.4Hz),
8.75(1H, s).

10 **Example 205**

Ethyl 2-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography
used in Example 204 was further flowed hexane-ethyl acetate
15 (3:1) as an eluent, the title compound (300 mg) was obtained
as colorless crystals.

MP:144-147°C.

Anal. Calcd. for: $C_{23}H_{28}ClN_3O_4$: C, 61.95; H, 6.33; N, 9.42.

Found: C, 61.93; H, 6.35; N, 9.40.

20 MS(EI): 445 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.85(3H, t, J=6.9Hz),
0.97(3H, t, J=7.3Hz), 1.49(9H, s), 1.63-1.69(2H, m), 2.66-
2.85(2H, m), 3.80(2H, q, J=6.9Hz), 5.57(1H, s), 7.10-7.15(1H, m),
7.17(1H, ddd, J=1.5, 7.3 and 7.8Hz), 7.23(1H, dd, J=6.4 and 7.3Hz),
25 7.41(1H, d, J=7.2Hz), 7.67(1H, s), 10.01(1H, s).

Example 206

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-methoxycarbonyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous
30 solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and methyl chloroformate in the same manner as in Example 204.
MS(EI): 403 (M^+).

IR(KBr): ν =3422, 1736, 1699, 1531, 1450, 1232, 1086 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.87(3H, t, J =7.1Hz),
0.97(3H, t, J =7.3Hz), 1.60-1.66(2H, m), 2.86-2.89(2H, m),
3.83(2H, q, J =7.1Hz), 3.94(3H, s), 5.55(1H, s), 7.13-7.38(4H, m),
5 7.35(1H, s), 8.67(1H, s).

Example 207

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-methoxycarbonyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography
10 used in Example 206 was further flowed hexane-ethyl acetate
(3:1) as an eluent, the title compound was obtained as
colorless crystals.

MP: 141-143°C.

MS(EI): 403(M^+).

15 IR(KBr): ν =3290, 1774, 1695, 1633, 1597, 1523, 1444, 1364, 1307, 1209
 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.86(3H, t, J =7.1Hz),
0.95(3H, t, J =7.3Hz), 1.64-1.70(2H, m), 2.71-2.85(2H, m),
3.78(2H, q, J =7.1Hz), 3.85(1H, s), 5.57(1H, s), 7.10-7.24(3H, m),
20 7.42(1H, d, J =1.4Hz), 7.72(1H, s), 9.94(1H, s).

Example 208

Ethyl 1-benzyloxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals
25 from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-
pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine
and benzyl chloroformate in the same manner as in Example 204.

MP: 80°C.

Anal. Calcd. for: $\text{C}_{26}\text{H}_{26}\text{ClN}_3\text{O}_4$: C, 65.07; H, 5.46; N, 8.75.

30 Found: C, 65.24; H, 5.71; N, 8.50.

MS(EI): 479(M^+).

IR(KBr): ν =3344, 1745, 1701, 1527, 1451, 1226, 1084, 1060 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, J =7.0Hz),

0.94(3H,t,J=7.3Hz), 1.56-1.62(2H,m), 2.81-2.88(2H,m),
3.82(2H,q,J=7.0Hz), 5.41(2H,s), 5.55(1H,s), 7.13-7.24(3H,m),
7.36(1H,s), 7.37(6H,m), 8.62(1H,s).

Example 209

5 Ethyl 2-benzyloxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Further elution using the column of silica gel column chromatography in Example 208 and hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless
10 amorphous solid.

MS(EI):479(M⁺).

IR(KBr): ν =3294,1759,1697,1601,1383,1363,1300,1201 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.85(3H,t,J=7.0Hz),
0.95(3H,t,J=7.3Hz), 1.61-1.67(2H,m), 2.72-2.82(2H,m),
15 3.79(2H,q,J=7.0Hz), 5.30(2H,s), 5.56(1H,s), 7.09-7.41(9H,m),
7.73(1H,s), 9.95(1H,s).

Example 210

Ethyl 1-benzoyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and benzoyl chloride in the same manner as in Example 204.

MP:115°C.

25 Anal. Calcd. for:C₂₅H₂₄ClN₃O₃:C,66.74;H,5.38;N,9.34.

Found:C,66.58;H,5.41;N,9.28.

MS(EI):449(M⁺).

IR(KBr): ν =3414,1680,1641,1516,1095 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.90(3H,t,J=6.3Hz),
30 1.00(3H,t,J=7.3Hz), 1.65-1.71(2H,m), 2.90-2.93(2H,m),
3.85(2H,q,J=7.3Hz), 5.63(1H,s), 7.16-7.22(2H,m),
7.29(1H,d,J=7.3Hz), 7.40(1H,d,J=7.8Hz), 7.46(1H,s), 7.50-
7.54(2H,m), 7.65(1H,dd,J=6.3 and 7.8Hz), 7.98(1H,d,J=6.3Hz),

9.10(1H,s).

Example 211

Ethyl 2-benzoyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 Through the column of silica gel column chromatography used in Example 210 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MP:119-121°C.

10 Anal. Calcd. for: C₂₅H₂₄ClN₃O₃: C, 66.74; H, 5.38; N, 9.34.

Found: C, 66.58; H, 5.43; N, 9.30.

MS(EI): 479(M⁺).

IR(KBr): v=3406, 1670, 1628, 1601, 1481, 1348, 1084 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=6.8Hz),

15 0.97(3H, t, J=7.3Hz), 1.65-1.67(2H, m), 2.74-2.83(2H, m),

3.82(2H, q, J=7.3Hz), 5.65(1H, s), 7.13-7.26(3H, m),

7.44(1H, d, J=7.8Hz), 7.47-7.51(2H, m), 7.60(1H, dd, J=7.3 and

7.3Hz), 7.91(2H, d, J=7.8), 8.00(1H, s), 10.06(1H, s).

Example 212

20 Ethyl 1-benzylcarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine

25 and phenylacetyl chloride in the same manner as in Example 204.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H, t, J=6.8Hz),

0.94(3H, t, J=7.3Hz), 1.60-1.61(2H, m), 2.84-2.86(2H, m),

3.82(2H, q, J=6.8Hz), 4.47(2H, s), 5.59(1H, s), 7.20-9.44(10H, m),

8.90(1H, s).

30 **Example 213**

Ethyl 2-benzylcarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography

used in Example 212 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MS(EI):463(M⁺).

5 IR(KBr): ν =3308,1699,1628,1630,1599,1523 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.87(3H,t,J=6.8Hz),
0.98(3H,t,J=7.3Hz), 1.65-1.71(2H,m), 2.77-2.84(2H,m),
3.83(2H,q,J=6.8Hz), 4.25(2H,s), 5.60(1H,s), 7.11-7.31(8H,m),
7.41(1H,d,J=7.8Hz), 7.84(1H,s), 10.30(1H,s).

10 **Example 214**

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-phenylcarbamoyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-
15 pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and phenyl isocyanate in the same manner as in Example 204.

MS(EI):464(M⁺).

IR(KBr): ν =3310,1699,1597,1518,1448,1369,1228,1194,1093 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.98(3H,t,J=7.1Hz),
20 0.97(3H,t,J=7.3Hz), 1.96(2H,m), 2.87(2H,m), 3.83(2H,q,J=7.1Hz),
5.61(1H,s), 7.11-7.69(8H,m), 7.67(2H,d,J=7.8Hz), 8.86(1H,s),
10.31(1H,s).

Example 215

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-phenylcarbamoyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

25 Through the column of silica gel column chromatography used in Example 214 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as colorless crystals.

30 MP:145-147°C.

Anal. Calcd. for:C₂₅H₂₅ClN₄O₃:C,64.58;H,5.42;N,12.05.

Found:C,64.10;H,5.41;N,12.30.

MS(EI):464(M⁺).

IR(KBr): $\nu=3341, 1697, 1653, 1630, 1597, 1520, 1367, 1197, 1093 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, $J=7.0\text{Hz}$),
0.97(3H, t, $J=7.3\text{Hz}$), 1.68(2H, m), 2.80-2.92(2H, m),
3.82(2H, q, $J=7.0\text{Hz}$), 5.62(1H, s), 7.10-7.20(3H, m),
5 7.22(1H, dd, $J=7.1$ and 7.1Hz), 7.31-7.33(2H, m),
7.41(1H, d, $J=7.1\text{Hz}$), 7.58-7.60(2H, m), 7.85(1H, s), 9.67(1H, s),
9.83(1H, s).

Example 216

Ethyl 1-benzylcarbamoyl-4-(2-chlorophenyl)-4,7-dihydro-6-
10 propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and benzyl isocyanate in the same manner as in Example 204.

15 MS(EI): 478(M^+).

IR(KBr): $\nu=3402, 1699, 1637, 1525, 1226, 1091 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, $J=7.0\text{Hz}$),
0.96(3H, t, $J=7.3\text{Hz}$), 1.61-1.63(2H, m), 2.83(2H, m),
3.82(2H, q, $J=7.0\text{Hz}$), 4.37(2H, d), 5.58(1H, s), 7.11-7.31(9H, m),
20 7.38(1H, d, $J=7.8\text{Hz}$), 8.74(1H, s), 9.01(1H, s).

Example 217

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-phenoxy carbonyl-6-
propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous
25 solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and phenyl chloroformate in the same manner as in Example 204.

MS(EI): 465(M^+).

IR(KBr): $\nu=3339, 1728, 1633, 1525, 1371, 1302, 1224, 1091 \text{ cm}^{-1}$.

30 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.83(3H, t, $J=7.1\text{Hz}$),
0.96(3H, t, $J=7.3\text{Hz}$), 1.70(2H, m), 2.94(2H, m), 3.82(2H, q, $J=7.1\text{Hz}$),
5.62(1H, s), 7.12-7.53(9H, m), 8.26(1H, s), 9.30(1H, s).

Example 218

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-phenoxy carbonyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 217 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as colorless crystals.

MP:156-157°C.

Anal. Calcd. for: C₂₅H₂₄ClN₃O₄: C, 64.44; H, 5.19; N, 9.02.

Found: C, 64.42; H, 5.31; N, 9.04.

10 MS(EI): 465(M⁺).

IR(KBr): ν=3325, 1765, 1685, 1597, 1525, 1373, 1205, 1099 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.1Hz),
1.00(3H, t, J=7.3Hz), 1.67-1.69(2H, m), 2.76-2.85(2H, m),
3.82(2H, q, J=7.1Hz), 5.61(1H, s), 7.15(1H, dd, J=1.7 and 6.8Hz),
15 7.15(1H, dd, J=1.7 and 6.8Hz), 7.17(1H, dd, J=2.0 and 7.6Hz),
7.24(1H, dd, J=1.3 and 7.4Hz), 7.27-7.31(3H, m), 7.41-7.45(3H, m),
7.89(1H, s), 10.01(1H, s).

Example 219

Ethyl 4-(2-chlorophenyl)-1-ethoxy carbonyl-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and ethyl chloroformate in the same manner as in Example 204.

25 MP:88-89°C.

Anal. Calcd. for: C₂₁H₂₄ClN₃O₄: C, 60.36; H, 5.79; N, 10.06.

Found: C, 60.24; H, 5.72; N, 10.05.

MS(EI): 417(M⁺).

IR(KBr): ν=3422, 1734, 1705, 1647, 1591, 1531, 1228, 1086, 1062 cm⁻¹.

30 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.1Hz),
0.96(3H, t, J=7.3Hz), 1.31(3H, t, J=7.1Hz), 1.61-1.66(2H, m), 2.83-
2.92(2H, m), 3.83(2H, q, J=7.1Hz), 4.41(2H, q, J=7.1Hz), 5.55(1H, s),
7.13-7.16(2H, m), 7.25(1H, dd, J=7.0 and 7.6Hz), 7.34(1H, s),

7.38(1H,d,J=7.6Hz), 8.65(1H,s).

Example 220

Ethyl 4-(2-chlorophenyl)-2-ethoxycarbonyl-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 Through the column of silica gel column chromatography used in Example 219 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MS(EI):417(M⁺).

10 IR(KBr): ν =3325,1765,1685,1631,1597,1525,1373,1205,1099 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.87(3H,t,J=7.1Hz),
0.97(3H,t,J=7.3Hz), 1.26(3H,t,J=7.0Hz), 1.63-1.69(2H,m), 2.74-
2.81(2H,m), 3.81(2H,q,J=7.1Hz), 4.29(2H,q,J=7.0Hz), 5.57(1H,s),
7.12(1H,dd,J=6.3 and 7.5Hz), 7.17(1H,d,J=7.8Hz),
15 7.23(1H,dd,J=6.3 and 7.4Hz), 7.40(1H,d,J=7.8Hz), 7.71(1H,s),
9.96(1H,s).

Example 221

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-propoxycarbonyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and propyl chloroformate in the same manner as in Example 204.
MP:66-68°C.

25 MS(EI):431(M⁺).

IR(KBr): ν =3356,1738,1695,1527,1282,1084 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.88(3H,t,J=7.0Hz),
0.92(3H,t,J=7.3Hz), 0.97(3H,t,J=7.3Hz), 1.62-1.67(2H,m), 1.70-
1.75(2H,m), 2.85-2.92(2H,m),3.83(2H,q,J=7.0Hz),
30 4.32(2H,t,J=6.5Hz), 5.57(1H,s), 7.14-7.18(2H,m),
7.26(1H,dd,J=6.3 and 7.6Hz), 7.35(1H,s), 7.39(1H,d,J=7.8Hz)
9.10(1H,s).

Example 222

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-propoxycarbonyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 221 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as colorless crystals.

MP:59°C.

Anal. Calcd. for: C₂₂H₂₆ClN₃O₄: C, 61.18; H, 6.07; N, 9.73.

Found: C, 60.81; H, 5.98; N, 9.74.

MS(EI): 431(M⁺).

IR(KBr): ν=3296, 1761, 1697, 1633, 1599, 1523, 1365, 1218, 1089 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.1Hz), 0.89(3H, t, J=7.5Hz), 0.97(3H, t, J=7.3Hz), 1.63-1.69(4H, m), 2.74-2.81(2H, m), 3.81(2H, q, J=7.1Hz), 4.21(2H, t, J=6.6Hz), 5.58(1H, s), 7.12(1H, dd, J=1.8 and 7.6Hz), 7.17(1H, ddd, J=1.9, 7.3 and 7.6Hz), 7.22(1H, ddd, J=1.2, 7.3 and 7.6Hz), 7.41(1H, dd, J=1.2 and 7.8Hz), 7.72(1H, s), 9.99(1H, s).

Example 223

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-isobutyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and isobutyryl chloride in the same manner as in Example 204.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.0Hz), 0.96(3H, t, J=7.3Hz), 1.10(3H, d, J=6.9Hz), 1.14(3H, d, J=6.8Hz), 1.64-1.70(2H, m), 2.75-2.83(2H, m), 3.53(1H, q, J=7.0Hz), 3.83(2H, t, J=6.9Hz), 5.59(1H, s), 7.12(1H, s), 7.16(1H, dd, J=5.8 and 7.8Hz), 7.24(1H, dd, J=6.3 and 7.5Hz), 7.41(1H, s), 7.81(1H, s), 10.05(1H, s).

Example 224

Ethyl 1-acetyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and acetyl chloride in the same manner as in Example 204.

5 MP:75-76°C.

Anal. Calcd. for: C₂₀H₂₂ClN₃O₃: C, 61.93; H, 5.72; N, 10.83.

Found: C, 61.77; H, 5.78; N, 10.90.

MS(EI): 387(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H, t, J=7.3Hz),
10 0.97(3H, t, J=7.3Hz), 1.60-1.66(2H, m), 2.66(3H, s), 2.85-
2.90(2H, m), 3.81(2H, q, J=7.3Hz), 5.57(1H, s), 7.14-7.18(2H, m),
7.26(1H, dd, J=7.3 and 7.6Hz), 7.38(1H, s), 7.39(1H, d, J=8.1Hz),
8.90(1H, s).

Example 225

15 Ethyl 2-acetyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 224 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a
20 colorless amorphous solid.

MS(EI): 387(M⁺).

IR(KBr): ν=3306, 1699, 1633, 1601, 1523, 1371, 1197, 1086 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.0Hz),
0.96(3H, t, J=7.3Hz), 1.66(2H, m), 2.44(3H, s), 2.65-2.85(2H, m),
25 3.80(2H, q, J=7.0Hz), 5.58(1H, s), 7.09-7.22(3H, m),
7.40(1H, d, J=7.9Hz), 7.80(1H, s), 10.0(1H, s).

Example 226

Ethyl 1-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and butyl chloroformate in the same manner as in Example 204.

MS(EI):445(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.87(3H, t, J=7.3Hz),
0.88(3H, t, J=7.1Hz), 1.33-1.38(2H, m), 1.60-1.69(4H, m), 2.85-
2.87(2H, m), 3.82(2H, q, J=7.3Hz), 4.36(2H, t, J=6.5Hz), 5.55(1H, s),
5 7.13-7.17(2H, m), 7.25(1H, dd, J=6.4 and 6.5Hz), 7.34(1H, s),
7.37(1H, d, J=7.5Hz), 8.61(1H, s).

Example 227

Ethyl 2-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

10 Through the column of silica gel column chromatography
used in Example 226 was further flowed hexane-ethyl acetate
(3:1) as an eluent, the title compound was obtained as a
colorless amorphous solid.

MS(EI):445(M⁺).

15 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.86(3H, t, J=7.3Hz),
0.87(3H, t, J=7.3Hz), 0.96(3H, t, J=7.3Hz), 1.31-1.32(2H, m),
1.61(4H, m), 2.73-2.80(2H, m), 3.80(2H, q, J=7.3Hz),
4.24(2H, t, J=6.5Hz), 5.57(1H, s), 7.09-7.22(3H, m),
7.39(1H, d, J=7.8Hz), 7.70(1H, s), 9.98(1H, s).

20 **Example 228**

Ethyl 4-(2-chlorophenyl)-1-cinnamoyl-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous
solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-
25 pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine
and cinnamoyl chloride in the same manner as in Example 204.

MP:131-134°C.

Anal. Calcd. for: C₂₇H₂₆ClN₃O₃: C, 68.13; H, 5.51; N, 8.83.

Found: C, 68.04; H, 5.58; N, 8.75.

30 MS(EI):475(M⁺).

IR(KBr): ν=3396, 1687, 1624, 1521, 1394, 1207, 1087 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.89(3H, t, J=7.0Hz),
0.98(3H, t, J=7.1Hz), 1.62-1.68(2H, m), 2.89-2.91(2H, m),

3.84(2H,q,J=7.0Hz), 5.60(1H,s), 7.16(1H,dd,J=7.4 and 7.8Hz),
7.18(1H,d,J=6.3Hz), 7.26(1H,dd,J=6.3 and 7.4Hz),
7.39(1H,d,J=7.8Hz), 7.45(1H,s), 7.46(3H,m), 7.67(1H,d,J=6.1Hz),
7.69-7.76(2H,m), 7.91(1H,d,J=7.4Hz), 9.01(1H,s).

5 **Example 229**

Ethyl 4-(2-chlorophenyl)-1-cinnamoyl-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 228 was further flowed hexane-ethyl acetate
10 (3:1) as an eluent, the title compound was obtained as colorless crystals.

MS(EI):475(M⁺).

IR(KBr): ν =3304,1695,1674,1601,1521,1365,1168,1095 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.86(3H,t,J=7.0Hz),
15 0.98(3H,t,J=7.3Hz), 1.65-1.70(2H,m), 2.76-2.87(2H,m),
3.82(2H,q,J=7.0Hz), 5.62(1H,s), 7.12-7.18(2H,m),
7.24(1H,dd,J=7.3 and 7.3Hz), 7.42(1H,d,J=7.8Hz), 7.45-
7.46(3H,m), 7.60(1H,d,J=6.1Hz), 7.62-7.70(2H,m),
7.86(1H,d,J=6.1Hz), 7.85(1H,s), 10.09(1H,s).

20 **Example 230**

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-3-methyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 2-ethylbenzaldehyde, 3-amino-5-methylpyrazol and ethyl 3-
25 ketohexanoate in the same manner as in Example 25.

MP:164-165°C.

MS(EI):359(M⁺).

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.94(3H,t,J=7.0Hz),
1.02(3H,t,J=7.3Hz), 1.61(2H,m), 1.89(3H,s), 2.60-2.85(2H,m),
30 3.80(2H,q,J=7.0Hz), 5.44(1H,s), 7.00-7.30(4H,m), 9.39(1H,s),
11.66(1H,s).

Example 231

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-methyl-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of ethyl 3-ketohexanoate (7.5 g), 2-chlorobenzaldehyde (6.6 g), piperidine (1.2 g) and acetic acid (2.25 g) in benzene (50 ml) was heated under reflux for 5 hours, and the reaction mixture was dehydrated using a Dean-Stark condenser. The solvent was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography using an eluent (hexane-ethyl acetate (3:1)) to give ethyl 2-(2-chlorophenyl)methylen-3-oxohexanoate ((E)/(Z)=1:1 mixture) as a yellow oil. A solution of ethyl 2-(2-chlorophenyl)methylene-3-oxohexanoate ((E)/(Z)=1:1 mixture, 2.8 g), 3-amino-1-methylpyrazole (0.25 g) and p-toluenesulfonic acid (25 mg) in toluene (5 mL) and dimethylsulfoxide (0.5 mL) was heated under reflux for one day. The solvent was evaporated under reduced pressure, and the mixture was extracted with ethyl acetate (10 mL) and washed with a saturated aqueous sodium chloride solution. The organic layer was dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent (ethyl acetate-methanol (10:1))) to give the title compound as colorless crystals.

MP:150-151°C.

MS(EI):359(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.83(3H, t, J=7.0Hz), 0.96(3H, t, J=6.5Hz), 1.65(2H, m), 2.67-2.85(2H, m), 3.58(3H, s), 3.77(2H, q, J=7.0Hz), 5.55(1H, s), 7.07-7.11(2H, m), 7.19(1H, dd, J=7.4 and 7.8Hz), 7.24(1H, d, J=8.3Hz), 9.45(1H, s).

Example 232

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-methyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 2-(2-chlorophenyl)methylen-3-oxohexanoate

((E)/(Z)=1:1 mixture), 3-amino-2-methylpyrazole and p-toluenesulfonic acid.

MS(EI):359(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.84(3H, t, J=7.0Hz),

5 1.00(3H, t, J=7.1Hz), 1.67-1.69(2H, m), 2.70-2.88(2H, m),
3.65(3H, s), 3.80(2H, q, J=7.0Hz), 5.55(1H, s), 6.96(1H, s), 7.08-
7.12(2H, m), 7.20(1H, dd, J=6.8 and 7.8Hz), 7.35(1H, d, J=7.8Hz),
9.31(1H, s).

Example 233

10 Ethyl 4,7-dihydro-1-methyl-4-(naphthalen-1-yl)-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of ethyl 3-ketohexanoate (6.6 g), 1-naphthaldehyde (7.34 g), piperidine (1.2 g) and acetic acid (2.25 g) in benzene (50 mL) was heated under reflux for 3
15 hours and the reaction mixture was dehydrated using a Dean-Stark condenser. The solvent was evaporated and the residue was purified by silica gel column chromatography using an eluent (hexane-ethyl acetate (3:1)) to give ethyl 2-(naphthalen-1-yl)methylene-3-oxohexanoate ((E)/(Z)=1:1
20 mixture) as a yellow oil. The title compound was obtained as a colorless amorphous solid from ethyl 2-(naphthalen-1-yl)methylene-3-oxohexanoate ((E)/(Z)=1:1 mixture), 3-amino-2-methylpyrazole and p-toluenesulfonic acid.

MS(EI):375(M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.60(3H, t, J=6.9Hz),
1.03(3H, t, J=6.9Hz), 1.74(2H, m), 2.78-2.85(2H, m), 3.65(3H, s),
3.68(2H, q, J=6.9Hz), 5.94(1H, s), 6.76(1H, s), 7.20(1H, d, J=7.3Hz),
7.37(1H, dd, J=7.4 and 7.8Hz), 7.50(1H, dd, J=6.9 and 7.8Hz),
7.58(1H, m), 7.67(1H, d, J=8.3Hz), 7.88(1H, d, J=8.3Hz),
30 8.42(1H, d, J=8.8Hz), 9.26(1H, s).

Example 234

Ethyl 4-(3-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 3-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:140-143°C.

5 Anal. Calcd. for: $C_{18}H_{20}ClN_3O_2 \cdot 2/5 H_2O$: C, 61.24; H, 5.94; N, 11.90.

Found: C, 61.50; H, 5.94; N, 11.99.

MS(EI): 345 (M^+).

IR(KBr): $\nu=3263, 1736, 1666, 1591, 1514, 1275, 1222, 1207, 1087 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, $J=7.0\text{Hz}$),

10 1.04(3H, t, $J=7.1\text{Hz}$), 1.58-1.63(2H, m), 2.63-2.81(2H, m),

3.86(2H, q, $J=7.0\text{Hz}$), 5.11(1H, s), 7.08(1H, d, $J=7.8\text{Hz}$), 7.12(2H, m),

7.21(1H, d, $J=8.3\text{Hz}$), 7.26(1H, s), 9.84(1H, s), 11.99(1H, s).

Example 235

Ethyl 4-(4-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-
15 b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 4-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:159-161°C.

20 Anal. Calcd. for: $C_{18}H_{20}ClN_3O_2 \cdot 1/5 H_2O$: C, 61.87; H, 5.88; N, 12.03.

Found: C, 61.92; H, 6.23; N, 11.95.

MS(EI): 345 (M^+).

IR(KBr): $\nu=3263, 1730, 1662, 1593, 1516, 1207, 1091 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, $J=7.0\text{Hz}$),

25 0.95(3H, t, $J=7.3\text{Hz}$), 1.60(2H, m), 2.64-2.80(2H, m),

3.84(2H, q, $J=7.0\text{Hz}$), 5.10(1H, s), 7.13(2H, d, $J=7.3\text{Hz}$), 7.22(1H, s),

7.25(2H, d, $J=7.3\text{Hz}$), 9.45(1H, s), 11.96(1H, s).

Example 236

Ethyl 4,7-dihydro-4-(4-methyl-1H-imidazol-5-yl)-6-propyl-2H-
30 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 4-methyl-5-imidazolecarboxaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:219-220°C.

Anal. Calcd. for: $C_{16}H_{21}N_5O_2 \cdot 1/2 H_2O$: C, 59.61; H, 6.25; N, 21.72.

Found: C, 59.34; H, 6.48; N, 22.06.

MS(EI): 315 (M^+).

5 IR(KBr): $\nu=3113, 2980, 1687, 1620, 1568, 1244, 1159 \text{ cm}^{-1}$.

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94(3H, t, $J=7.3\text{Hz}$),
1.08(3H, t, $J=7.0\text{Hz}$), 1.58-1.59(2H, m), 2.21(3H, s), 2.58-
2.79(2H, m), 3.97(2H, q, $J=7.3\text{Hz}$), 5.50(1H, s), 6.14(1H, s),
7.14(1H, s), 7.19(1H, s), 9.78(1H, s), 11.53(1H, s).

10 **Example 237**

Ethyl 4,7-dihydro-4-(1-methyl-1H-imidazol-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 1-methyl-2-imidazolecarboxaldehyde, 3-aminopyrazole and
15 ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:209°C.

Anal. Calcd. for: $C_{16}H_{21}N_5O_2 \cdot 3/5 H_2O$: C, 59.28; H, 6.28; N, 21.60.

Found: C, 59.00; H, 6.52; N, 21.55.

MS(EI): 315 (M^+).

20 IR(KBr): $\nu=3254, 3184, 3080, 1685, 1593, 1518, 1278, 1207, 1078 \text{ cm}^{-1}$.

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, $J=6.8\text{Hz}$),
0.93(3H, t, $J=7.3\text{Hz}$), 1.55-1.61(2H, m), 2.57-2.80(2H, m),
3.44(3H, s), 3.87(2H, q, $J=6.8\text{Hz}$), 5.29(1H, s), 6.56(1H, s),
6.84(1H, s), 7.27(1H, s), 9.38(1H, s), 11.97(1H, s).

25 **Example 238**

Ethyl 4,7-dihydro-4-(1H-imidazol-5-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 3-imidazolecarboxyaldehyde, 3-aminopyrazole and ethyl 3-
30 ketohexanoate in the same manner as in Example 25.

MP:200°C.

Anal. Calcd. for: $C_{15}H_{17}N_5O_2 \cdot 1/2 H_2O$: C, 58.43; H, 5.88; N, 22.71.

Found: C, 58.53; H, 6.25; N, 22.93.

MS(EI):301(M⁺).

IR(KBr): ν =3217,1655,1585,1506,1226,1205,1084 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.92(3H,t,J=7.3Hz),
1.01(3H,t,J=7.3Hz), 1.57-1.59(2H,m), 2.59-2.74(2H,m),
5 3.90(2H,q,J=7.3Hz), 5.12(1H,s), 6.35(1H,s), 7.35(1H,s),
7.38(1H,s), 9.21(1H,s), 11.91(1H,s).

Example 239

Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-butyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

10 The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 1.

MP:213°C.

Anal. Calcd. for:C₁₉H₂₁N₅O₃:C,62.11;H,5.76;N,19.06.

15 Found:C,62.08;H,5.75;N,18.95.

MS(EI):367(M⁺).

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.77(3H,t,J=7.3Hz),
0.92(3H,t,J=7.3Hz), 1.32-1.40(2H,m), 1.60-1.64(2H,m), 2.76-
2.86(2H,m), 3.76-3.82(2H,m), 5.68(1H,s), 7.11(1H,d,J=6.6Hz),
20 7.22(1H,s), 7.51(1H,dd,J=9.0Hz and 6.6Hz), 7.77(1H,d,J=9.0Hz),
9.65(1H,s), 12.00(1H,s).

Example 240

Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

25 The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-ketopentanoate in the same manner as in Example 1.

MP:196°C.

Anal. Calcd. for:C₁₇H₁₇N₅O₃:C,60.17;H,5.05;N,20.64.

30 Found:C,60.09;H,5.15;N,20.41.

MS(EI):339(M⁺).

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.75 (3H,t, J=7.3Hz), 1.21 (3H,t, J=7.3Hz), 2.83(2H,q,J=7.3Hz), 3.73-3.84(2H,m), 5.68(1H,s),

7.12(1H,d,J=6.6Hz), 7.22(1H,s), 7.50(1H,dd,J=9.0Hz and 6.6Hz),
7.77(1H,d,J=9.0Hz), 9.68(1H,s), 12.01(1H,s).

Example 241

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-
5 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:174°C.

10 Anal. Calcd. for: C₁₇H₁₁ClN₄S 1/10 H₂O: C, 59.94; H, 3.31; N, 16.45.
Found: C, 59.82; H, 3.48; N, 16.93.

MS(EI): 338(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.50(1H,s), 7.18(1H,dd,J=7.3Hz
and 7.2Hz), 7.24-7.35(4H,m), 7.45(1H,d,J=7.8Hz),
15 7.60(1H,d,J=3.6Hz), 7.77(1H,d,J=3.9Hz), 10.08(1H,s),
12.29(1H,s).

Example 242

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(thiophen-2-yl)-2H-
20 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:215°C.

Anal. Calcd. for: C₁₈H₁₄N₄OS: C, 64.65; H, 4.22; N, 16.75.

25 Found: C, 64.66; H, 4.32; N, 17.02.

MS(EI): 334(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.85(3H,s), 5.34(1H,s),
6.93(1H,dd,J=7.3Hz and 7.2Hz), 7.01(1H,d,J=7.3Hz), 7.14-
7.25(4H,m), 7.60(1H,d,J=3.6Hz), 7.77(1H,d,J=5.1Hz), 9.91(1H,s),
30 12.17(1H,s).

Example 243

5-Cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-(thiophen-2-yl)-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:222°C.

5 Anal. Calcd. for: $C_{18}H_{14}N_4S_2 \cdot 2/5 H_2O$: C, 60.44; H, 4.17; N, 15.66.

Found: C, 60.58; H, 4.44; N, 15.35.

MS(EI): 350 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.49(3H, s), 5.48(1H, s), 7.17-7.28(5H, m), 7.33(1H, d, J=7.3Hz), 7.60(1H, d, J=3.7Hz),

10 7.77(1H, d, J=3.9Hz), 10.01(1H, s), 12.22(1H, s).

Example 244

5-Cyano-4,7-dihydro-4-(2-nitrophenyl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:165°C.

Anal. Calcd. for: $C_{17}H_{11}N_5O_2S$: C, 58.44; H, 3.17; N, 20.05.

Found: C, 58.15; H, 3.42; N, 20.38.

20 MS(EI): 349 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54(1H, s), 7.18(1H, dd, J=7.3Hz and 7.2Hz), 7.34(1H, s), 7.48-7.55(2H, m), 7.60(1H, d, J=3.7Hz), 7.72-7.79(2H, m), 7.92(1H, d, J=8.1Hz), 10.16(1H, s), 12.35(1H, s).

25 Example 245

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2,1,3-benzothiadiazol-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:254°C.

Anal. Calcd. for: $C_{17}H_{10}N_6S_2$: C, 56.34; H, 2.78; N, 23.19.

Found: C, 56.01; H, 2.91; N, 23.19.

MS(EI):362(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 5.84(1H,s), 7.19(1H,dd,J=4.4Hz and 4.3Hz), 7.28(1H,s), 7.55(1H,d,J=6.8Hz), 7.65(1H,d,J=3.7Hz), 7.72-7.79(2H,m), 7.99(1H,d,J=8.8Hz), 10.14(1H,s), 12.21(1H,s).

5 **Example 246**

5-Cyano-4,7-dihydro-4-(naphthalen-1-yl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, naphthalene-1-aldehyde and 3-aminopyrazole in the
10 same manner as in Example 95.

MP:214°C.

Anal. Calcd. for:C₂₁H₁₄N₄S:C,71.16;H,3.98;N,15.81.

Found:C,70.75;H,3.96;N,15.85.

MS(EI):354(M⁺).

15 ¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 5.87(1H,s),7.13(1H,s),
7.18(1H,dd,J=4.6Hz and 3.9Hz), 7.45-7.54(4H,m),
7.62(1H,d,J=3.9Hz), 7.78(1H,d,J=4.9Hz), 7.83(1H,d,J=8.1Hz),
7.95(1H,d,J=9.3Hz), 8.31(1H,d,J=7.3Hz), 10.09(1H,s),
12.17(1H,s).

20 **Example 247**

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in
25 the same manner as in Example 95.

MP:232°C.

Anal. Calcd. for:C₁₇H₁₀Cl₂N₄S 1/10 H₂O:C,54.44;H,2.74;N,14.94.

Found:C,54.08;H,2.90;N,15.29.

MS(EI):373(M⁺).

30 ¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 5.58(1H,s), 7.18(1H,dd,J=7.3Hz and 7.2Hz), 7.32-7.41(3H,m), 7.54(1H,dd,J=7.3Hz and 1.5Hz),
7.60(1H,d,J=3.7Hz), 7.78(1H,d,J=4.9Hz), 10.14(1H,s),
12.32(1H,s).

Example 248

5-Cyano-4,7-dihydro-4-(2-methylphenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-methylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:246°C.

Anal. Calcd. for: C₂₀H₁₆N₄ 1.0 H₂O: C, 72.71; H, 5.49; N, 16.96.

Found: C, 72.50; H, 5.26; N, 17.20.

10 MS(EI): 312(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.38(3H, s), 5.29(1H, s), 7.11-7.23(5H, m), 7.47-7.49(3H, m), 7.55-7.58(2H, m), 9.94(1H, s), 12.17(1H, s).

Example 249

15 5-Cyano-4,7-dihydro-4-(2-methylphenyl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-methylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

20 MP:276°C.

Anal. Calcd. for: C₁₈H₁₄N₄S: C, 67.90; H, 4.43; N, 17.60.

Found: C, 67.93; H, 4.54; N, 17.64.

MS(EI): 318(M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.36(3H, s), 5.28(1H, s), 7.11-7.18(5H, m), 7.24(1H, s), 7.55(1H, dd, J=3.7Hz and 1.0Hz), 7.74(1H, dd, J=5.9Hz and 1.0Hz), 9.95(1H, s), 12.22(1H, s).

Example 250

4-(2-Chlorophenyl)-5-cyano-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl dimethoxyacetate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.39(6H, s), 5.18(1H, s),

5.43(1H,s), 7.23-7.27(3H,m), 7.32-7.35(1H,m),
7.44(1H,d,J=7.8Hz), 9.65(1H,s), 12.21(1H,s).

Example 251

4-(2-Chlorophenyl)-5-cyano-6-formyl-4,7-dihydro-2H-

5 pyrazolo[3,4-b]pyridine

4-(2-Chlorophenyl)-5-cyano-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (4.4 g) was added to trifluoroacetic acid (20 ml) under ice-cooling and the mixture was stirred at room temperature for 2.5 hours. The reaction
10 mixture was concentrated under reduced pressure and crystallized from ethyl acetate (50 ml) to give the title compound (1.9 g) as yellow crystals.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 5.63(1H,s), 7.27-7.46(5H,m),
7.48(1H,d,J=7.1Hz), 9.73(1H,s), 10.17(1H,s), 12.34(1H,s).

15 Example 252

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-
pyrazolo[3,4-b]pyridine

To a suspension of 4-(2-chlorophenyl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (400 mg) in methanol
20 (10 ml) was added sodium borohydride (53 mg) under ice-cooling and the mixture was stirred at the same temperature for 30 minutes. 10% Hydrochloric acid was added to the reaction mixture, and a saturated sodium hydrogencarbonate solution was added. The precipitated crystals were collected by filtration
25 and washed with ethanol to give the title compound (295 mg) as yellow crystals.

MP:205-210°C (decomposition).

Anal. Calcd. for: C₁₄H₁₁ClN₄O 1/4 H₂O: C, 57.74; H, 3.98; N, 19.24.

Found: C, 57.38; H, 3.93; N, 18.94.

30 MS(EI): 286 (M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 4.29(2H,d,J=5.6Hz), 5.38(1H,s),
5.49(1H,t,J=5.6Hz), 7.22-7.34(4H,m), 7.43(1H,d,J=8.0Hz),
9.60(1H,s), 12.17(1H,s).

Example 253

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(trans-2-ethoxycarbonylethenyl)-2H-pyrazolo[3,4-b]pyridine

To a suspension of sodium hydride (94 mg) in
5 dimethoxyethane (10 ml) was added ethyl
diethylphosphonoacetate (528 mg) and the mixture was stirred
at room temperature for 15 minutes. Under ice-cooling, 4-(2-
chlorophenyl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-
b]pyridine (670 mg) was added to the mixture, and the mixture
10 was stirred at the same temperature for 1 hour. Water was
added to the reaction mixture and the mixture was extracted
with ethyl acetate. The extract was washed with a saturated
aqueous sodium chloride solution and dried over anhydrous
magnesium sulfate. The solvent was evaporated and the obtained
15 residue was purified by silica gel column chromatography
(eluent: hexane-ethyl acetate (1:1)) to give the title
compound (560 mg) as yellow crystals.

MP:240-243°C (decomposition).

Anal. Calcd. for: $C_{18}H_{15}ClN_4O_2 \cdot 1/2 H_2O$: C, 59.43; H, 4.43; N, 15.40.

20 Found: C, 59.53; H, 4.26; N, 15.31.

MS(EI): 354 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.25(3H, d, J=7.1Hz),
4.21(2H, q, J=7.1Hz), 5.52(1H, s), 6.93(1H, d, J=15.9Hz), 7.27-
7.46(6H, m), 10.09(1H, s), 12.31(1H, s).

25 Example 254

4-(2-Chlorophenyl)-5-cyano-6-(2-ethoxycarbonylethyl)-4,7-
dihydro-2H-pyrazolo[3,4-b]pyridine

A suspension of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-
6-(trans-2-ethoxycarbonylethenyl)-2H-pyrazolo[3,4-b]pyridine
30 (260 mg) and 5% palladium on carbon (110 mg) in ethanol was
subjected to catalytic hydrogenation at room temperature for 5
hours. The reaction mixture was filtered through Celite and
the filtrate was concentrated under reduced pressure. The

obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give a yellow solid. The yellow solid was crystallized from ethyl acetate-diisopropyl ether to give the title compound (160 mg) as pale-yellow crystals.

MP: 172-174°C.

MS(EI): 356(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.18(3H, t, J=7.3Hz), 2.60-2.80(4H, m), 4.08(2H, q, J=7.3Hz), 5.35(1H, s), 7.20-7.31(4H, m), 7.42(1H, d, J=8.0Hz), 9.84(1H, s), 12.16(1H, s).

Example 255

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl dimethoxyacetate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.35(3H, s), 3.38(3H, s), 5.16(1H, s), 5.47(1H, s), 7.26(1H, s), 7.42(1H, d, J=6.6Hz), 7.60(1H, dd, J=6.6, 8.5Hz), 7.94(1H, d, J=8.5Hz), 9.77(1H, s), 12.19(1H, s).

Example 256

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 251.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.71(1H, s), 7.33(1H, s), 7.56(1H, d, J=6.6Hz), 7.62(1H, dd, J=6.6, 8.8Hz), 7.98(1H, d, J=8.8Hz), 9.73(1H, s), 10.32(1H, s), 12.32(1H, s).

Example 257

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-

benzoxadiazol-4-yl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 252. MP:215-220°C (decomposition).

Anal. Calcd. for: $C_{14}H_{10}N_6O_2 \cdot 1/2 H_2O$: C, 55.44; H, 3.66; N, 27.71.

5 Found: C, 55.32; H, 3.68; N, 27.31.

MS(EI): 294 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 4.30(2H, s), 5.45(1H, s), 5.52(1H, brs), 7.27(1H, s), 7.42(1H, d, J=6.6Hz), 7.59(1H, dd, J=6.6, 9.0Hz), 7.93(1H, d, J=9.0Hz), 9.71(1H, s),

10 12.16(1H, s).

Example 258

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(trans-2-ethoxycarbonylethenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 253.

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.24(3H, d, J=7.1Hz), 4.21(2H, q, J=7.1Hz), 5.59(1H, s), 6.96(1H, d, J=16.1Hz), 7.32(1H, s), 7.39(1H, d, J=16.1Hz), 7.50(1H, m), 7.59(1H, m), 7.96(1H, d, J=8.3Hz), 10.21(1H, s), 12.29(1H, s).

Example 259

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(2-ethoxycarbonylethyl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(trans-2-ethoxycarbonylethenyl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 254.

MS(EI): 364 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.18(3H, t, J=7.1Hz), 2.66-2.80(4H, m), 4.08(2H, q, J=7.1Hz), 5.40(1H, s), 7.26(1H, s), 7.42(1H, d, J=6.6Hz), 7.58(1H, dd, J=6.6, 9.0Hz), 7.92(1H, d, J=9.0Hz), 9.96(1H, s), 12.16(1H, s).

Example 260

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₇H₁₄BrN₅: C, 55.45; H, 3.83; N, 19.02.

Found: C, 55.30; H, 3.91; N, 18.98.

MS(EI): 368(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.23(3H, d, J=6.8Hz), 1.27(3H, d, J=6.8Hz), 3.03(1H, m), 5.45(1H, s), 7.33(1H, s), 7.55-7.82(2H, m), 7.83(1H, dd, J=2.0, 7.1Hz), 9.76(1H, s), 12.25(1H, s).

Example 261

4-(2-Bromophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine acetonitrile

The title compound was prepared from methyl isobutyrate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₆H₁₅BrN₄C₂H₃N: C, 56.26; H, 4.72; N, 18.22.

Found: C, 56.05; H, 4.56; N, 17.09.

MS(EI): 343(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.24(3H, d, J=7.1Hz), 1.27(3H, d, J=7.1Hz), 2.06(3H, s), 3.06(1H, m), 5.23(1H, s), 7.13-7.18(1H, m), 7.22(1H, d, J=7.6Hz), 7.27(1H, s), 7.36(1H, dd, J=1.2, 7.6Hz), 7.59(1H, dd, J=1.2, 8.0Hz), 9.64(1H, s), 12.17(1H, s).

Example 262

5-Cyano-4,7-dihydro-6-isopropyl-4-(2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 224°C.

MS (EI): 309 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.23 (3H, d, J=7.1Hz),
1.28 (3H, d, J=7.1Hz), 3.03 (1H, m), 5.36 (1H, s), 7.27 (1H, s), 7.43-
5 7.49 (2H, m), 7.70 (1H, dd, J=1.2, 8.8Hz), 7.89 (1H, dd, J=1.2, 8.3Hz),
9.71 (1H, s), 12.23 (1H, s).

Example 263

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-isopropyl-2H-
pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl isobutyrate,
2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: >250°C.

Anal. Calcd. for: C₁₆H₁₄Cl₂N₄: C, 57.67; H, 4.23; N, 16.89.

15 Found: C, 57.74; H, 4.27; N, 16.89.

MS (EI): 333 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.23 (3H, d, J=7.1Hz),
1.27 (3H, d, J=7.1Hz), 3.04 (1H, m), 5.42 (1H, s), 7.23 (1H, d, J=7.6Hz),
7.31 (1H, s), 7.35 (1H, dd, J=7.6, 7.8Hz), 7.51 (1H, dd, J=1.5, 7.8Hz),
20 9.70 (1H, s), 12.21 (1H, s).

Example 264

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-isopropyl-
2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl isobutyrate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 94.

MP: 222-223°C (decomposition).

Anal. Calcd. for: C₁₆H₁₄N₆O: C, 62.71; H, 4.61; N, 27.44.

Found: C, 62.71; H, 4.65; N, 27.45.

30 MS (EI): 306 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.24 (3H, d, J=7.1Hz),
1.25 (3H, d, J=7.1Hz), 3.03 (1H, m), 5.39 (1H, s), 7.26 (1H, s),
7.40 (1H, d, J=6.6Hz), 7.58 (1H, dd, J=6.6, 8.8Hz),

7.92(1H,d,J=8.8Hz), 9.74(1H,s), 12.15(1H,s).

Example 265

5-Cyano-4,7-dihydro-6-isopropyl-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl isobutyrate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₇H₁₈N₄O: C, 69.37; H, 6.16; N, 19.03.

10 Found: C, 69.13; H, 6.21; N, 19.54.

MS(EI): 294(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.23(3H,d,J=7.1Hz),
1.28(3H,d,J=7.1Hz), 3.09(1H,m), 3.83(3H,s), 5.19(1H,s),
6.90(1H,dd,J=7.4,7.6Hz), 6.99(1H,d,J=7.6Hz),
15 7.05(1H,dd,J=1.7,7.4Hz), 7.15-7.19(2H,m), 9.47(1H,s),
12.04(1H,s).

Example 266

4-(2-Chlorophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl cyclopropanecarboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₆H₁₃ClN₄: C, 64.76; H, 4.42; N, 18.88.

25 Found: C, 64.71; H, 4.50; N, 19.05.

MS(EI): 296(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89-0.93(2H,m), 1.00-1.15(2H,m),
2.01(1H,m), 5.35(1H,s), 7.22-7.26(3H,m), 7.31-7.34(1H,m),
7.42(1H,d,J=7.8Hz), 9.14(1H,s), 12.16(1H,s).

30 **Example 267**

4-(2-Bromophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl

cyclopropanecarboxylate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₆H₁₃BrN₄: C, 56.32; H, 3.84; N, 16.42.

5 Found: C, 56.18; H, 3.90; N, 16.48.

MS(EI): 341(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-0.93(2H, m), 1.00-1.15(2H, m), 2.01(1H, m), 5.34(1H, s), 7.13-7.22(2H, m), 7.27(1H, s), 7.34-7.38(1H, m), 7.59(1H, d, J=6.8Hz), 9.15(1H, s), 12.16(1H, s).

10 **Example 268**

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine 1/4 acetonitrile

The title compound was prepared from methyl cyclopropanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₇H₁₂BrN₅H₂O 1/4 CH₃CN: C, 53.28; H, 3.77; N, 18.64.

Found.: C, 53.28; H, 3.72; N, 18.81.

MS(EI): 366(M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-0.93(2H, m), 1.03-1.08(2H, m), 1.96-2.00(1H, m), 5.45(1H, s), 7.32(1H, s), 7.54-7.60(2H, m), 7.83(1H, dd, J=1.7, 7.1Hz), 9.27(1H, s), 12.25(1H, s).

Example 269

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopropanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 200-201°C (decomposition).

30 Anal. Calcd. for: C₁₆H₁₂N₆O H₂O: C, 59.62; H, 4.38; N, 26.07.

Found: C, 59.93; H, 4.05; N, 26.19.

MS(EI): 304(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88-0.93(2H, m), 1.01-1.12(2H, m),

1.99(1H,m), 5.39(1H,s), 7.25(1H,s), 7.40(1H,d,J=6.6Hz),
7.59(1H,dd,J=6.6,9.0Hz), 7.92(1H,d,J=9.0Hz), 9.26(1H,s),
12.15(1H,s).

Example 270

5 4-(2-Methoxyphenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine 1/4 acetonitrile

The title compound was prepared from methyl
cyclopropanecarboxylate, 2-methoxybenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

10 MP:241-243°C.

Anal. Calcd. for: C₁₇H₁₆N₄O 1/4 CH₃CN: C, 69.46; H, 5.58; N, 19.67.

Found: C, 69.35; H, 5.56; N, 19.64.

MS(EI): 292(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-0.92(2H,m), 0.99-1.10(2H,m),
15 2.01-2.06(1H,m), 3.84(3H,s), 5.21(1H,s),
6.90(1H,dd,J=7.3,7.6Hz), 6.98-7.05(2H,m), 7.15-7.19(2H,m),
8.97(1H,s), 12.04(1H,s).

Example 271

5-Cyano-6-cyclopropyl-4-(2,3-dichlorophenyl)-4,7-dihydro-2H-
20 pyrazolo[3,4-b]pyridine 1/4 acetonitrile

The title compound was prepared from methyl
cyclopropanecarboxylate, 2,3-dichlorobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP: >250°C.

25 Anal. Calcd. for: C₁₆H₁₂Cl₂N₄ 1/4 CH₃CN: C, 58.04; H, 3.76; N, 17.43.

Found: C, 57.87; H, 3.79; N, 17.44.

MS(EI): 331(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-0.93(2H,m), 1.03-1.08(2H,m),
1.98-2.03(1H,m), 5.43(1H,s), 7.22(1H,d,J=7.8Hz), 7.31(1H,s),
30 7.35(1H,t,J=7.8Hz), 7.51(1H,dd,J=1.5,7.8Hz), 9.21(1H,s),
12.20(1H,s).

Example 272

5-Cyano-6-cyclopropyl-4,7-dihydro-4-(2-nitrophenyl)-2H-

pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopropanecarboxylate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

5 MP:236-238°C (decomposition).

Anal. Calcd. for: C₁₆H₁₃N₅O₂: C, 62.53; H, 4.26; N, 22.79.

Found: C, 62.54; H, 4.29; N, 22.85.

MS(EI): 307(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-0.93(2H, m), 1.01-1.09(2H, m),
10 1.99(1H, m), 5.37(1H, s), 7.27(1H, s), 7.42-7.49(2H, m),
7.70(1H, dd, J=7.5, 7.6Hz), 7.90(1H, d, J=8.1Hz), 9.23(1H, s),
12.22(1H, s).

Example 273

Ethyl 4-(2-chlorophenyl)-6-dimethoxymethyl-4,7-dihydro-2H-

15 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 4,4-dimethoxy-3-oxobutanoate in the same manner as in Example 1.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.1Hz), 3.35(3H, s),
20 3.46(3H, s), 3.82(2H, m), 5.64(1H, s), 6.11(1H, s), 7.10-7.14(2H, m),
7.20-7.24(1H, m), 7.27(1H, s), 7.36(1H, d, J=8.3Hz), 8.94(1H, s),
12.05(1H, s).

Example 274

Ethyl 4-(2-chlorophenyl)-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-

25 b]pyridine-5-carboxylate

To a solution of ethyl 4-(2-chlorophenyl)-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (463 mg) in tetrahydrofuran (5 ml) was added 1N hydrochloric acid (10 ml) and the mixture was stirred at room
30 temperature for 6 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and

dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (290 mg) as a yellow solid.

5 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, $J=7.3\text{Hz}$), 3.91(2H, m), 5.70(1H, s), 7.14-7.24(3H, m), 7.31(1H, s), 7.40(1H, d, $J=7.8\text{Hz}$), 9.64(1H, s), 10.23(1H, s), 12.19(1H, s).

Example 275

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

2-Chlorobenzaldehyde (1.41 g), 3-aminopyrazole (0.83 g) and ethyl isobutyrylacetate (1.58 g) were stirred in acetic acid (10 ml) at 80°C for 2 hours. Under ice-cooling, a saturated aqueous sodium hydrogencarbonate solution was added to the reaction mixture. The insoluble material was filtered off, and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The extract was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)). The purified product was crystallized from hexane-ethyl acetate to give the title compound (115 mg) as white crystals.

MP: 211-213°C.

25 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.85(3H, t, $J=7.1\text{Hz}$), 1.16(3H, m), 1.28(3H, d, $J=7.1\text{Hz}$), 3.76(2H, m), 4.35(1H, m), 5.59(1H, s), 7.07-7.13(2H, m), 7.18-7.22(1H, m), 7.24(1H, s), 7.35(1H, dd, $J=1.2, 8.1\text{Hz}$), 9.14(1H, s), 11.97(1H, s).

Example 276

30 Ethyl 4-(2-bromophenyl)-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-bromobenzaldehyde, 3-aminopyrazole and ethyl isobutyrylacetate in the same manner

as in Example 275.

MP:214-215°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=6.8Hz), 1.16(3H, m), 1.28(3H, d, J=6.8Hz), 3.76(2H, m), 4.35(1H, m), 5.56(1H, s), 7.07-
5 7.13(2H, m), 7.02(1H, dd, J=7.3, 7.8Hz), 7.11(1H, d, J=6.4Hz), 7.24(1H, dd, J=7.4, 7.8Hz), 7.28(1H, s), 7.52(1H, d, J=7.8Hz), 9.15(1H, s), 11.98(1H, s).

Example 277

Ethyl 4-(2-chlorophenyl)-6-cyclopropyl-4,7-dihydro-2H-
10 pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 2-oxazolydone (20.8 g) in tetrahydrofuran (750 ml) was added n-butyllithium (1.56 M hexane solution, 153 ml) at -78°C and the mixture was stirred at the same temperature for 30 minutes. To the reaction
15 mixture was added a solution of cyclopropanecarbonyl chloride (25 g) in tetrahydrofuran (50 ml) at -78°C over 30 minutes. The mixture was stirred for 14 hours while gradually raising the temperature to room temperature. The reaction mixture was poured into ice-water and the mixture was extracted with ethyl
20 acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The extract was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give
25 white crystals (26 g). A mixture of the obtained white crystals (10 g), ethyl bromoacetate (21.5 ml) and zinc powder (25.3 g) in tetrahydrofuran (300 ml) was ultrasonicated for 2 hours and heated under reflux for 2 hours. To the reaction mixture was added 10% hydrochloric acid and the insoluble
30 material was filtered off through Celite. The filtrate was extracted with ethyl acetate, and the extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The extract was concentrated

under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give ethyl 3-cyclopropyl-3-oxopropionate (5.7 g) as a yellow oil. Subsequently, the title compound was
5 prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-cyclopropyl-3-oxopropionate in the same manner as in Example 275.

MP:190-192°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.83-0.93(4H, m), 1.10(1H, m),
10 3.14(1H, m), 3.80(2H, m), 5.60(1H, s), 7.08-7.12(2H, m), 7.18-7.22(1H, m), 7.25(1H, s), 7.34(1H, d, J=8.3Hz), 8.62(1H, s), 11.99(1H, s).

Example 278

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine
15

The title compound was prepared from methyl thiophene-2-carboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:>280°C.

20 Anal. Calcd. for: C₁₈H₁₀BrN₅S: C, 52.95; H, 2.47; N, 17.15.

Found: C, 52.72; H, 2.69; N, 17.21.

MS(EI): 408(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.62(1H, s), 7.18(1H, dd, J=5.1Hz and 3.7Hz), 7.40(1H, s), 7.59-7.67(3H, m), 7.79(1H, d, J=3.9Hz),
25 7.86(1H, dd, J=7.6Hz and 2.0Hz), 10.20(1H, s), 12.37(1H, s).

Example 279

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-methyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate 2-chlorobenzaldehyde and 3-amino-5-methylpyrazole in the same
30 manner as in Example 94.

MP:260°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.91(3H, t, J=7.3Hz), 1.60-

1.65(2H,m), 1.71(3H,s), 2.33(2H,q,J=7.3Hz), 5.27(1H,s), 7.20-7.24(2H,m), 7.31(1H,dd,J=7.3Hz and 7.2Hz), 7.39(1H,d,J=7.3Hz), 9.68(1H,s), 11.83(1H,s).

Example 280

5 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-phenyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate 2-chlorobenzaldehyde and 3-amino-5-phenylpyrazole in the same manner as in Example 94.

10 MP:262°C.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.89(3H,t,J=7.3Hz), 1.61-1.63(2H,m), 2.36(2H,q,J=7.3Hz), 5.61(1H,s), 7.09-7.34(9H,m), 9.89(1H,s), 12.62(1H,s).

Example 281

15 1-tert-Butoxycarbonyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine

The title compound was obtained as a colorless amorphous solid from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and di-tert-
20 butyl dicarbonate in the same manner as in Example 204.

MP:98-102°C.

MS(EI):398(M⁺).

IR(KBr):ν=3391,2199,1723,1643,1529,1394,1149 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.95(3H,t,J=7.3Hz), 1.57(3H,s),
25 1.60-1.67(2H,m), 2.53-2.61(2H,m), 5.38(1H,s), 7.25-7.31(3H,m), 7.35(1H,ddd,J=1.4,7.3 and 7.8Hz), 7.45(1H,d,J=8.1Hz), 9.20(1H,s).

Example 282

30 2-tert-Butoxycarbonyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

Through the column of silica gel column chromatography used in Example 281 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as

colorless crystals.

MP:175°C (decomposition).

Anal. Calcd. for: C₂₁H₂₃ClN₄O₂: C, 63.23; H, 5.81; N, 14.05.

Found: C, 62.91; H, 5.80; N, 13.82.

5 MS(EI): 398(M⁺).

IR(KBr): ν =3329, 2197, 1747, 1612, 1523, 1369, 1311, 1151, 949 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.93(3H, t, J=7.4Hz),
1.65(2H, q, J=7.3Hz), 2.40-2.44(2H, m), 2.48(9H, s), 5.32(1H, s),
7.27-7.36(3H, m), 7.45(1H, d, J=7.8Hz), 7.68(1H, s), 10.32(1H, s).

10 **Example 283**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-1-phenylcarbamoyl-6-propyl-1H-pyrazolo[3,4-b]pyridine

The title compound was obtained as a colorless amorphous solid from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and phenyl isocyanate in the same manner as in Example 204.

MP:138-140°C.

Anal. Calcd. for: C₂₃H₂₀ClN₅O 1/4 H₂O: C, 65.4; H, 4.89; N, 16.58.

Found: C, 65.20; H, 5.05; N, 16.17

20 MS(EI): 417(M⁺).

IR(KBr): ν =3387, 3294, 2202, 1712, 1537 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.95(3H, t, J=7.3Hz),
1.63(2H, q, J=7.4Hz), 2.58(2H, m), 5.43(1H, s), 7.13(1H, dd, J=7.4
and 7.5Hz), 7.24-7.36(6H, m), 7.46(1H, d, J=7.8Hz),
25 7.69(2H, d, J=7.8Hz), 9.46(1H, s), 10.38(1H, s).

Example 284

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-2-phenylcarbamoyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

Through the column of silica gel column chromatography used in Example 283 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless oil.

MP:167-171°C.

MS(EI): 417 (M^+).

IR(KBr): $\nu=3215, 2204, 1732, 1631, 1523, 1375 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.97(3H, t, $J=7.4\text{Hz}$),
1.65(2H, q, $J=7.3\text{Hz}$), 2.48(2H, m), 5.39(1H, s), 6.95(1H, dd, $J=7.3$
5 and 7.3Hz), 7.11(2H, dd, $J=7.3$ and 7.6Hz), 7.24-7.49(4H, m),
7.61(2H, d, $J=7.8\text{Hz}$), 7.88(1H, s), 8.63(1H, s), 9.77(1H, s),
10.17(1H, s).

Example 285

2-Acetoxyacetyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-
10 propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine, dimethylaminopyridine and
acetoxyacetyl chloride in the same manner as in Example 204.

15 MP: 149-150°C.

Anal. Calcd. for: $\text{C}_{20}\text{H}_{19}\text{ClN}_4\text{O}_3$: C, 60.23; H, 4.80; N, 14.05.

Found: C, 60.17; H, 4.83; N, 13.90.

MS(EI): 398 (M^+).

IR(KBr): $\nu=3281, 3238, 2197, 1745, 1630, 1608, 1523, 1385, 1344, 1236,$
20 1172 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, $J=7.3\text{Hz}$), 1.64-
1.70(2H, m), 2.44(2H, q, $J=7.3\text{Hz}$), 3.33(3H, s), 5.26(2H, s),
5.37(1H, s), 7.29-7.35(3H, m), 7.46(1H, d, $J=7.8\text{Hz}$), 7.86(1H, s),
10.45(1H, s).

25 **Example 286**

Ethyl 1-acetoxyacetyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-
1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals
from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-
30 pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine
and acetoxyacetyl chloride in the same manner as in Example
204.

MP: 130-131°C.

Anal. Calcd. for: $C_{22}H_{24}ClN_3O_5$: C, 59.26; H, 5.43; N, 9.42.

Found: C, 59.17; H, 5.39; N, 9.31.

MS(EI): 445 (M^+).

IR(KBr): $\nu=3337, 1732, 1529, 1390, 1246, 1086 \text{ cm}^{-1}$.

5 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, $J=7.0\text{Hz}$),
0.97(3H, t, $J=7.3\text{Hz}$), 1.64–1.70(2H, m), 2.76–2.82(2H, m),
3.31(3H, s), 3.85(2H, q, $J=7.0\text{Hz}$), 5.27(2H, dd, $J=3.0$ and 9.8Hz),
5.60(1H, s), 7.10–7.25(3H, m), 7.41(1H, dd, $J=1.4$ and 8.0Hz),
7.82(1H, s), 10.1(1H, s).

10 **Example 287**

Ethyl 1-benzylcarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and phenylacetyl chloride in the same manner as in Example 204.

MS(EI): 463 (M^+).

IR(KBr): $\nu=3418, 1701, 1521, 1392, 1228 \text{ cm}^{-1}$.

15 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, $J=7.0\text{Hz}$),
0.93(3H, t, $J=7.3\text{Hz}$), 1.57–1.62(2H, m), 2.80–2.87(2H, m),
3.82(2H, q, $J=7.0\text{Hz}$), 4.33(2H, s), 5.57(1H, s), 7.15(1H, dd, $J=7.4$
and 7.8Hz), 7.18–7.31(7H, m), 7.39(1H, d, $J=7.8\text{Hz}$), 7.44(1H, s),
8.94(1H, s).

Example 288

25 4-(2,1,3-Benzoxadiazol-4-yl)-2-tert-butoxycarbonyl-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and tert-butyldicarbonate in the same manner as in Example 204.

MP: 168–170°C.

Anal. Calcd. for: $C_{21}H_{22}N_6O_3$: C, 62.06; H, 5.46; N, 20.68.

Found: C, 61.92; H, 5.44; N, 20.52.

MS(EI): 406(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H, t, J=7.3Hz), 1.47(9H, s),
1.65(2H, m), 2.40(2H, m), 5.39(1H, s), 7.49(1H, d, J=6.3Hz),
7.60(1H, dd, J=6.6 and 9.0Hz), 7.79(1H, s), 7.96(1H, d, J=6.6Hz),
5 10.43(1H, s).

Example 289

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-1-phenylcarbamoyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
10 from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and phenyl isocyanate in the same manner as in Example 204.

MP: 138-140°C.

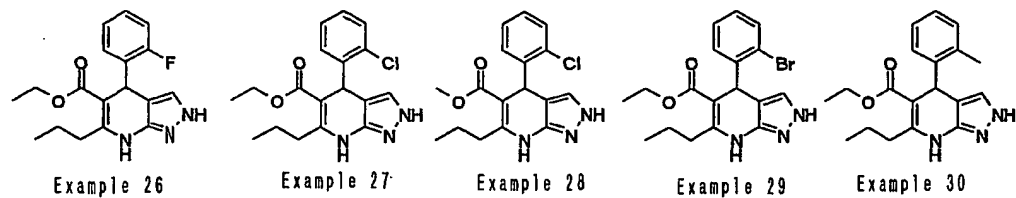
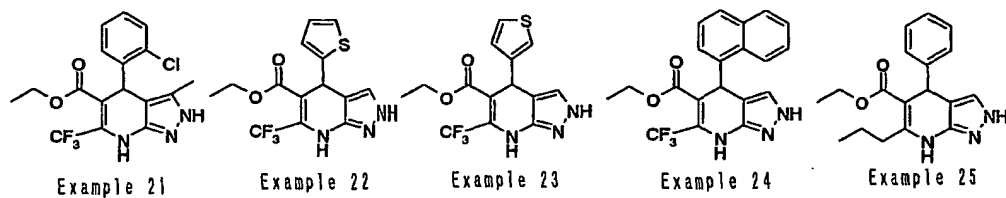
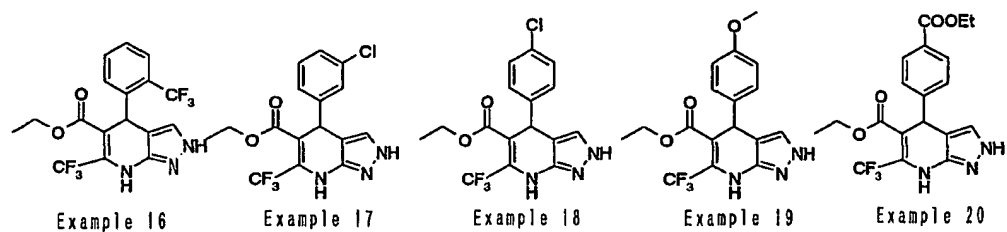
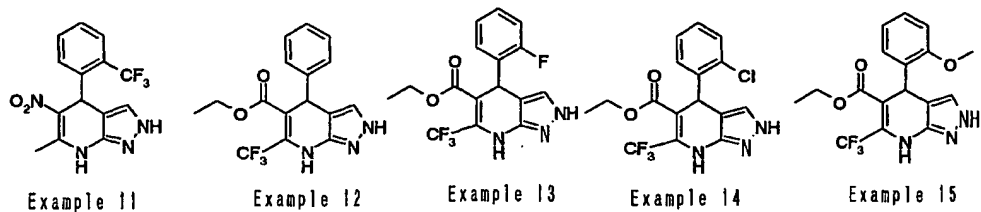
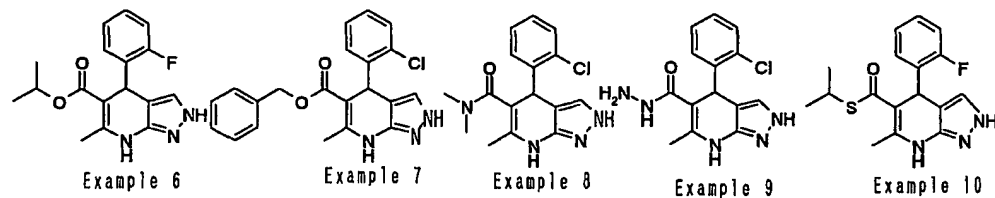
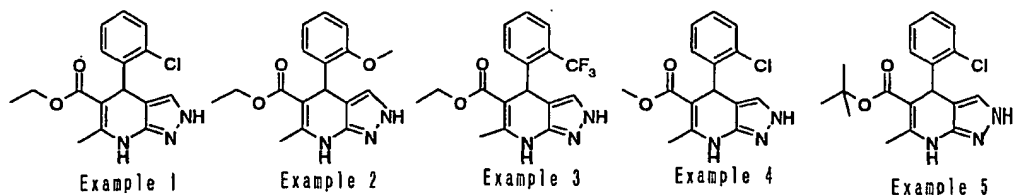
Anal. Calcd. for: C₂₃H₁₉N₇O₂: C, 64.93; H, 4.50; N, 23.05.

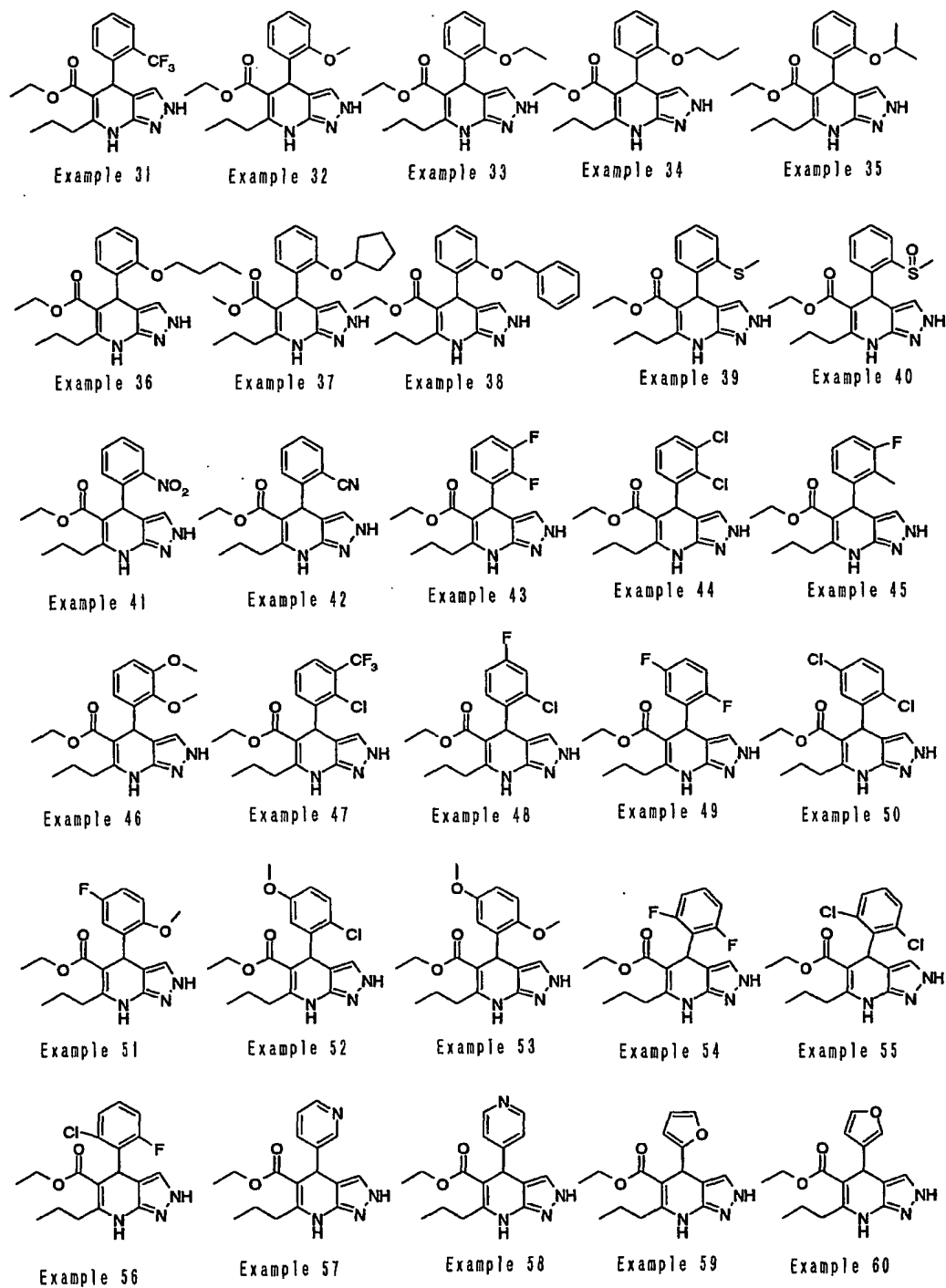
15 Found: C, 65.07; H, 5.05; N, 21.24.

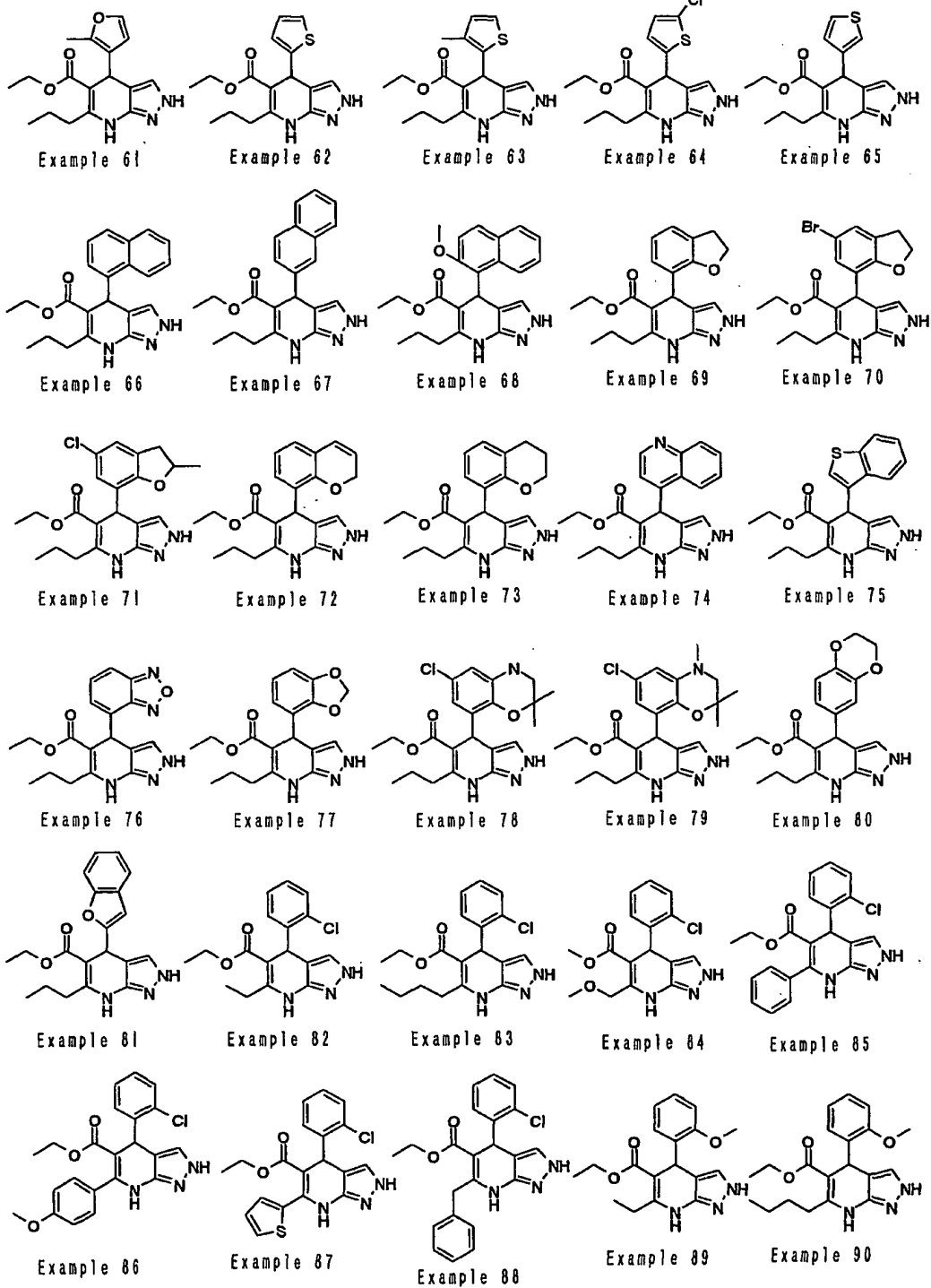
MS(EI): 425(M⁺).

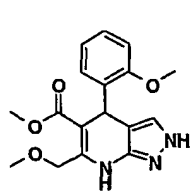
¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.91(3H, t, J=7.3Hz), 1.62(2H, m),
2.58(2H, m), 5.47(1H, s), 7.13(1H, dd, J=6.3 and 6.6Hz), 7.32-
7.39(3H, m), 7.49(1H, d, J=6.5Hz), 7.61-7.91(3H, m),
20 7.98(1H, d, J=9.1Hz), 9.54(1H, s), 10.34(1H, s).

The compounds of the above-described Examples are as follows.

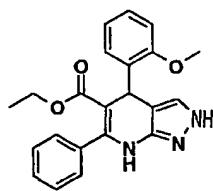




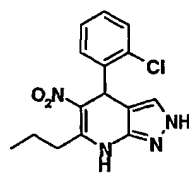




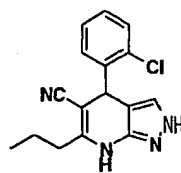
Example 91



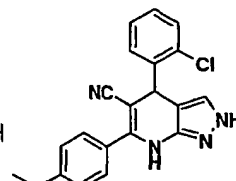
Example 92



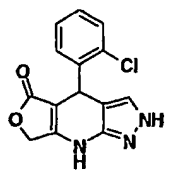
Example 93



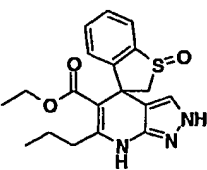
Example 94



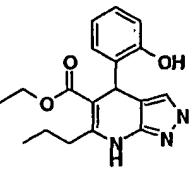
Example 95



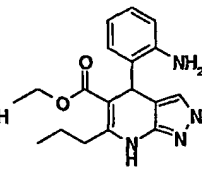
Example 96



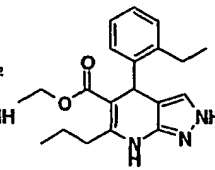
Example 97



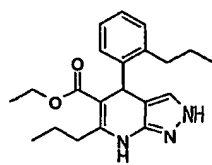
Example 98



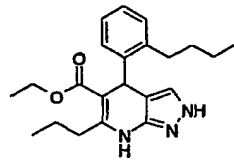
Example 99



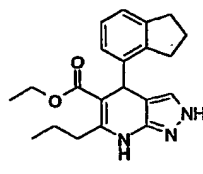
Example 100



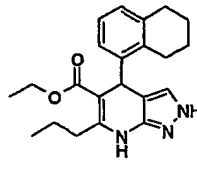
Example 101



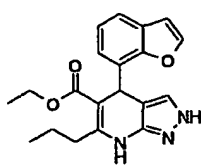
Example 102



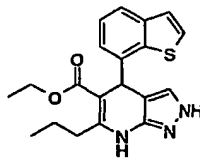
Example 103



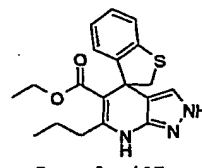
Example 104



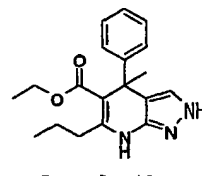
Example 105



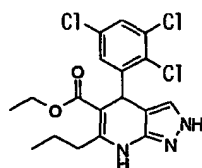
Example 106



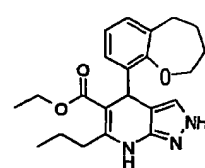
Example 107



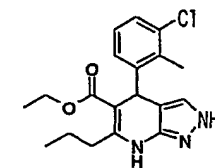
Example 108



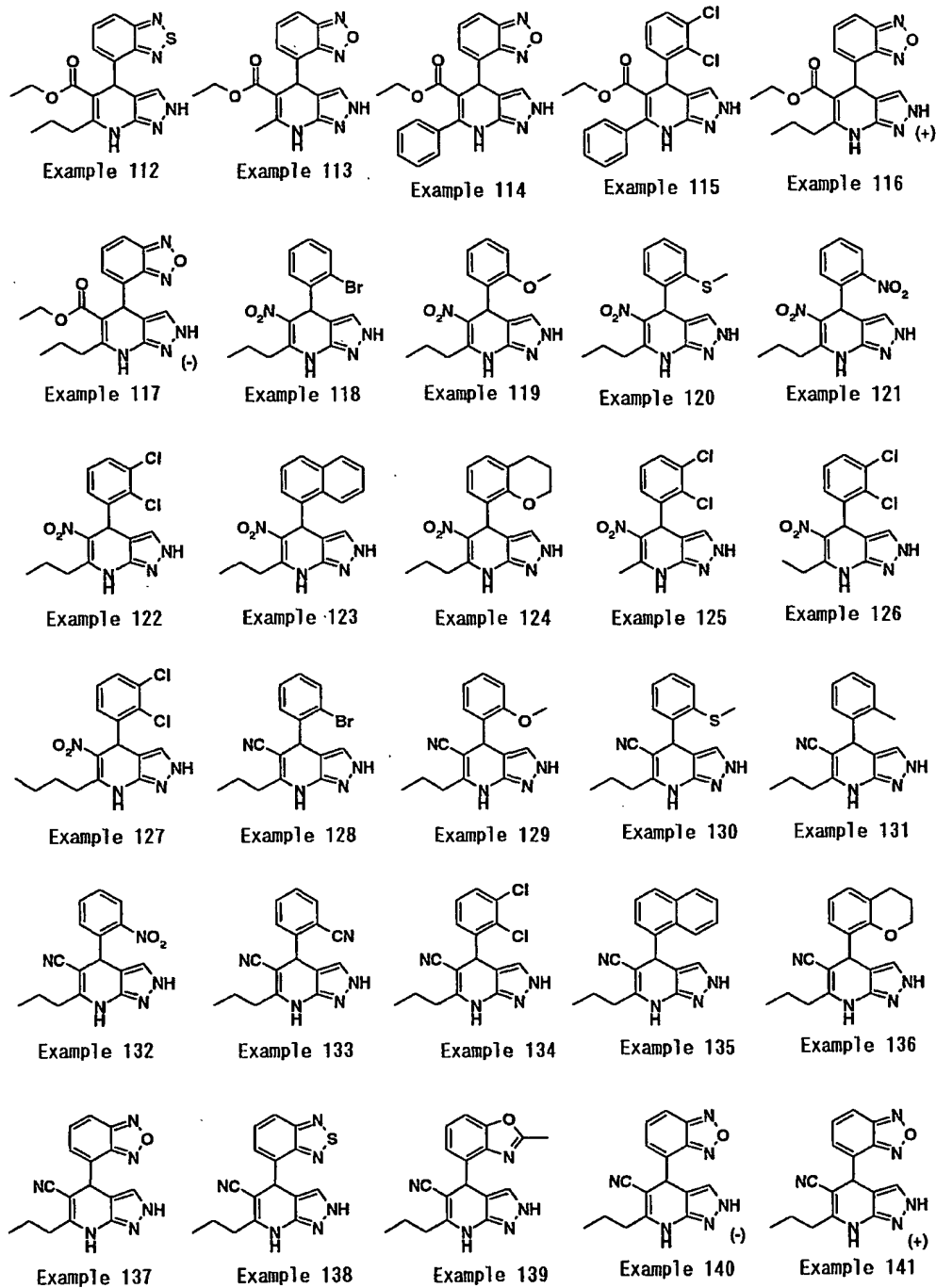
Example 109

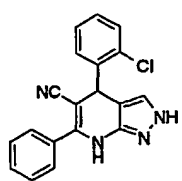


Example 110

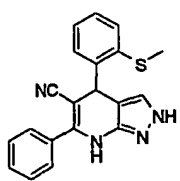


Example 111

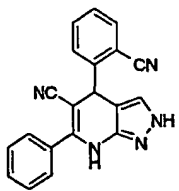




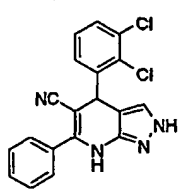
Example 142



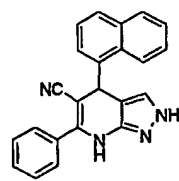
Example 143



Example 144



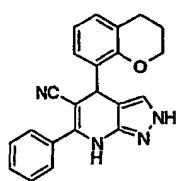
Example 145



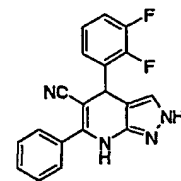
Example 146



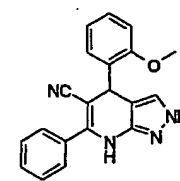
Example 147



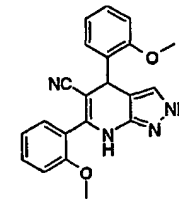
Example 148



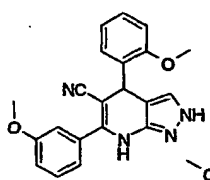
Example 149



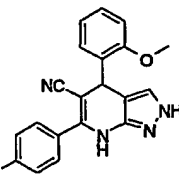
Example 150



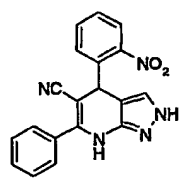
Example 151



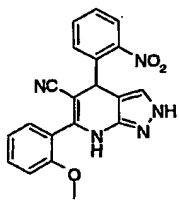
Example 152



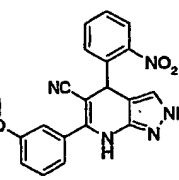
Example 153



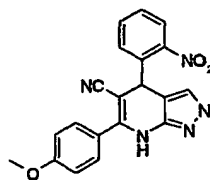
Example 154



Example 155



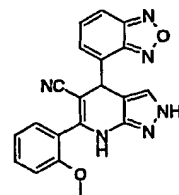
Example 156



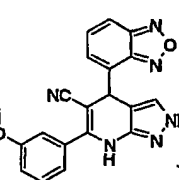
Example 157



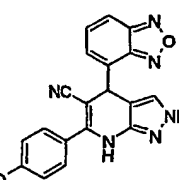
Example 158



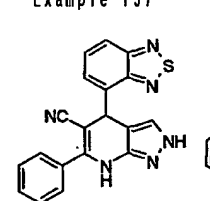
Example 159



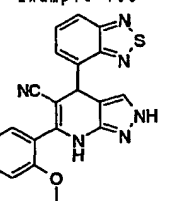
Example 160



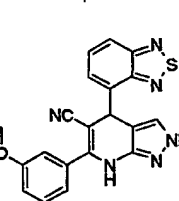
Example 161



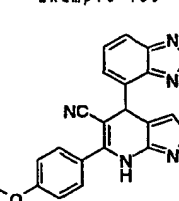
Example 162



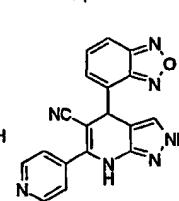
Example 163



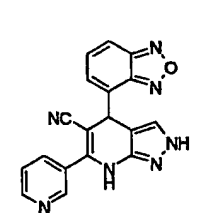
Example 164



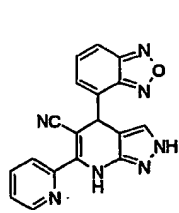
Example 165



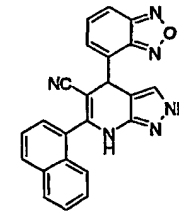
Example 166



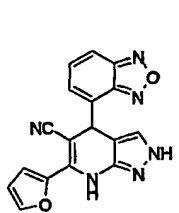
Example 167



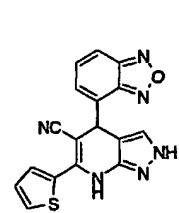
Example 168



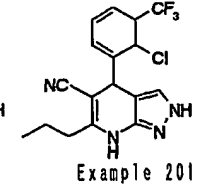
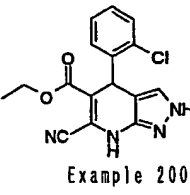
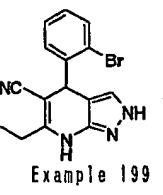
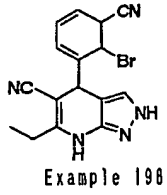
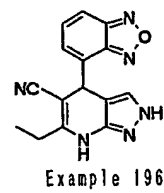
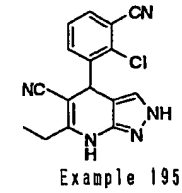
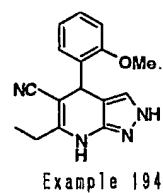
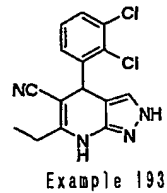
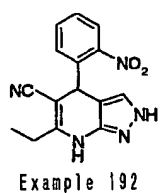
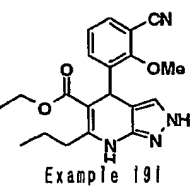
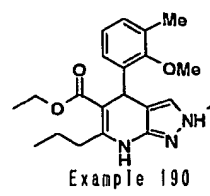
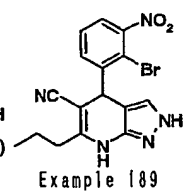
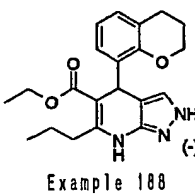
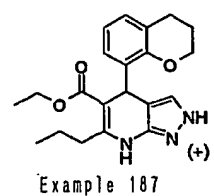
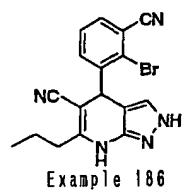
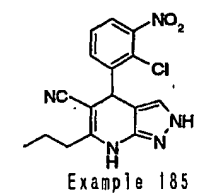
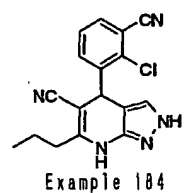
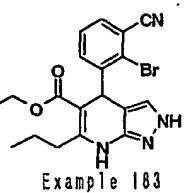
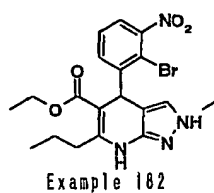
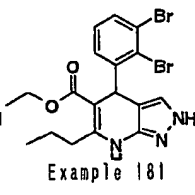
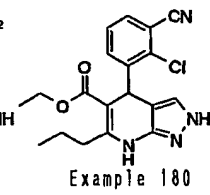
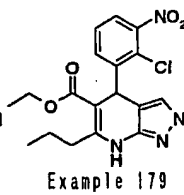
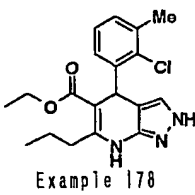
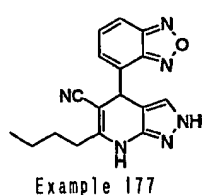
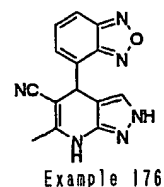
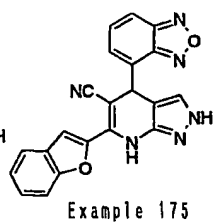
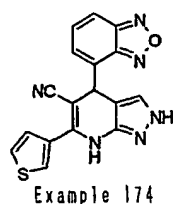
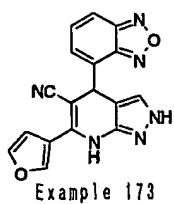
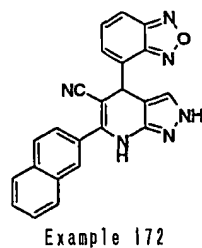
Example 169

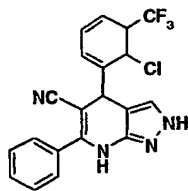


Example 170

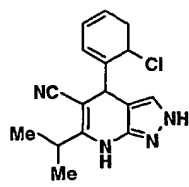


Example 171

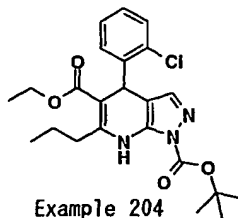




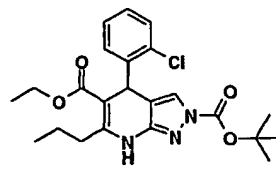
Example 202



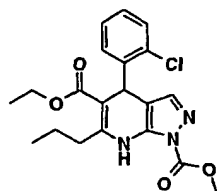
Example 203



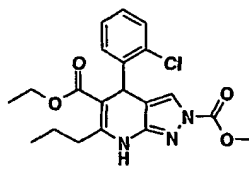
Example 204



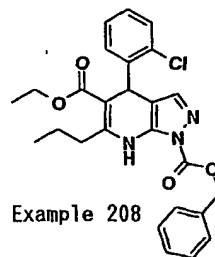
Example 205



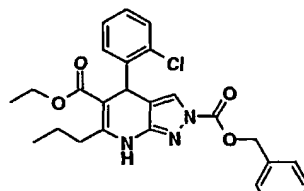
Example 206



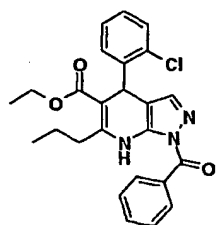
Example 207



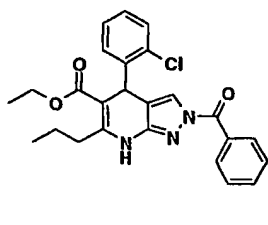
Example 208



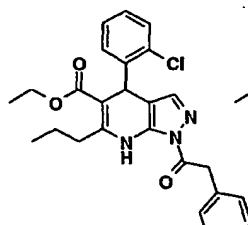
Example 209



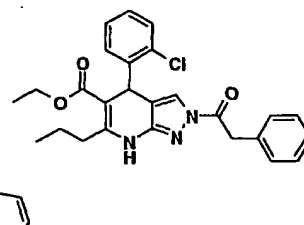
Example 210



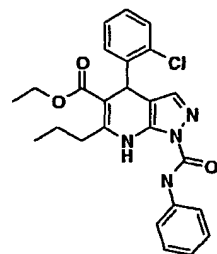
Example 211



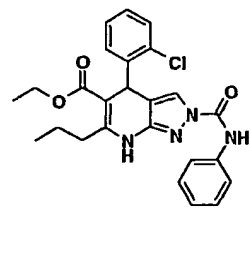
Example 212



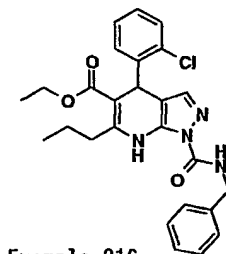
Example 213



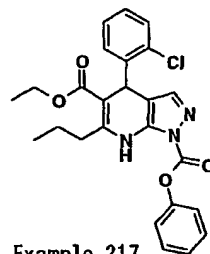
Example 214



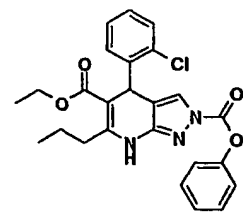
Example 215



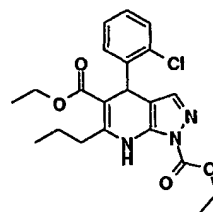
Example 216



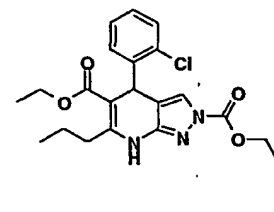
Example 217



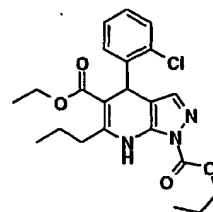
Example 218



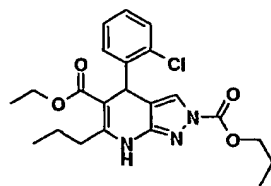
Example 219



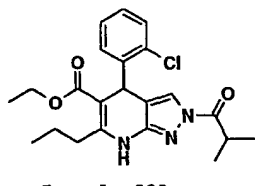
Example 220



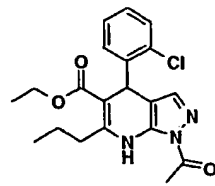
Example 221



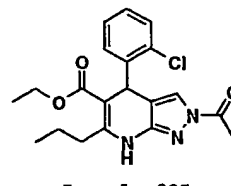
Example 222



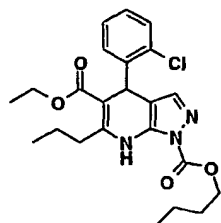
Example 223



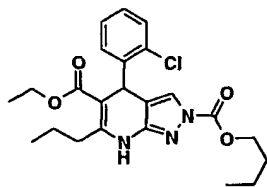
Example 224



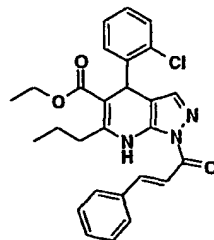
Example 225



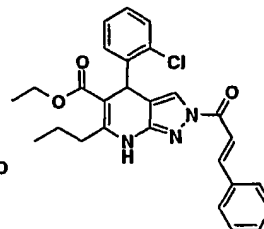
Example 226



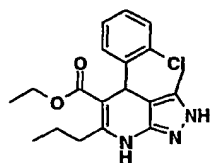
Example 227



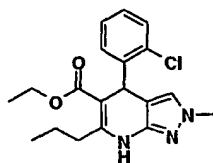
Example 228



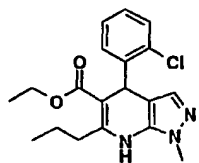
Example 229



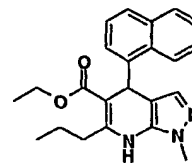
Example 230



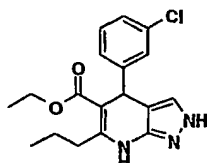
Example 231



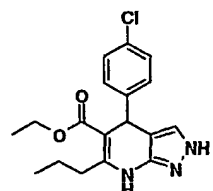
Example 232



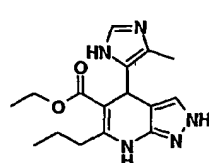
Example 233



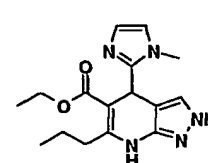
Example 234



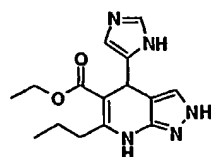
Example 235



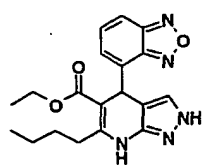
Example 236



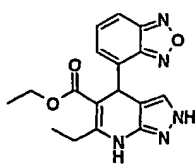
Example 237



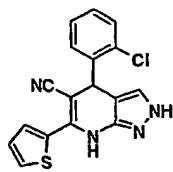
Example 238



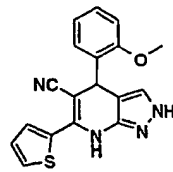
Example 239



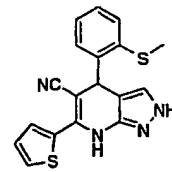
Example 240



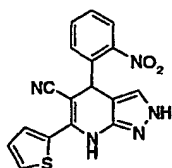
Example 241



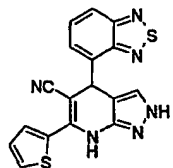
Example 242



Example 243



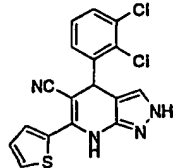
Example 244



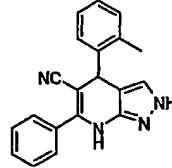
Example 245



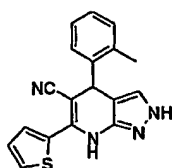
Example 246



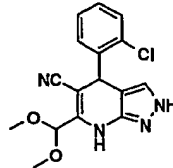
Example 247



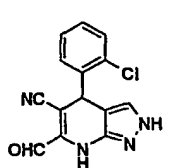
Example 248



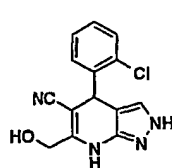
Example 249



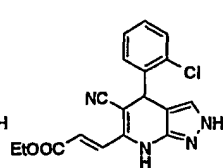
Example 250



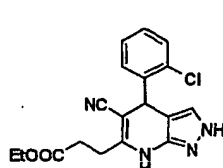
Example 251



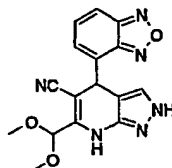
Example 252



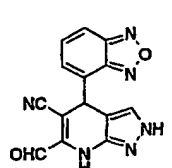
Example 253



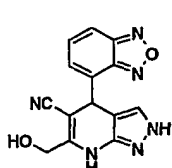
Example 254



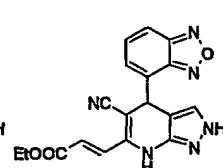
Example 255



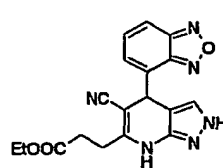
Example 256



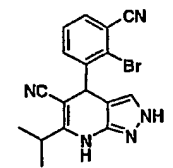
Example 257



Example 258



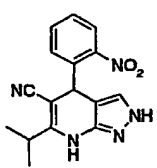
Example 259



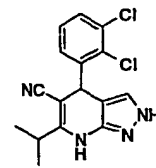
Example 260



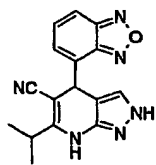
Example 261



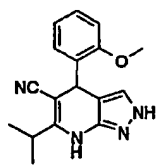
Example 262



Example 263



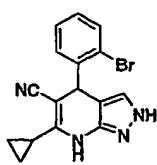
Example 264



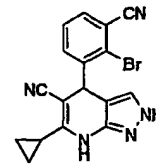
Example 265



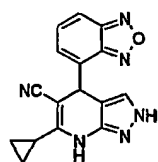
Example 266



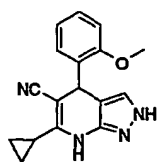
Example 267



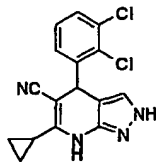
Example 268



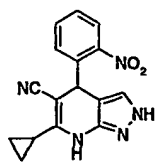
Example 269



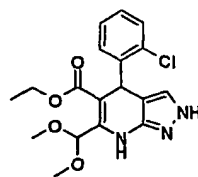
Example 270



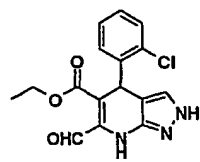
Example 271



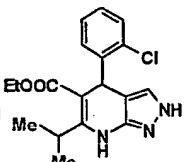
Example 272



Example 273



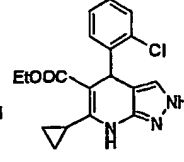
Example 274



Example 275



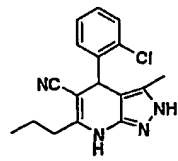
Example 276



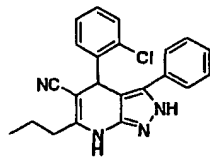
Example 277



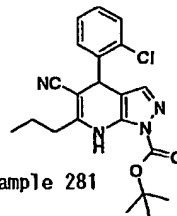
Example 278



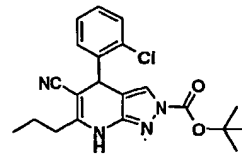
Example 279



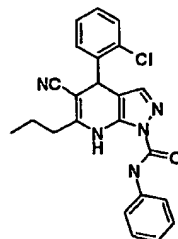
Example 280



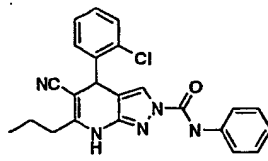
Example 281



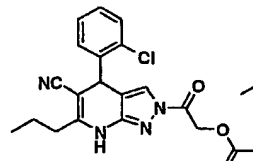
Example 282



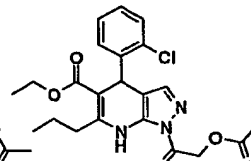
Example 283



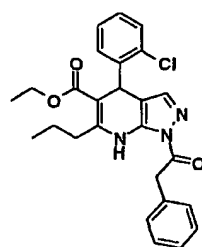
Example 284



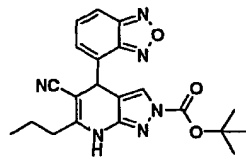
Example 285



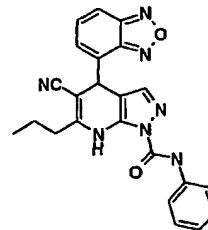
Example 286



Example 287



Example 288



Example 289

Example 2904-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(4-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (15 g) in DMSO (25 mL) was
5 added methyl p-anisate (25 g) and the mixture was stirred with
heating at 60°C for 1 hour. The reaction mixture was allowed
to cool and cold water (100 mL) was added dropwise. The
mixture was acidified with hydrochloric acid and the
precipitated crystals were collected by filtration. The
10 obtained crystals were extracted with ethyl acetate and the
solvent was evaporated under reduced pressure. The residue was
recrystallized from ethyl acetate to give 4-
methoxybenzoylacetonitrile (21 g) as colorless crystals. To a
solution of the obtained crystals in toluene was added
15 hydrazine monohydrate (13 g) and the mixture was heated under
reflux for 3 hours. The mixture was cooled and the
precipitated crystals were collected by filtration to give 5-
amino-3-(4-methoxyphenyl)pyrazole (22 g). Subsequently, the
title compound was prepared from methyl butyrate, 2-
20 chlorobenzaldehyde and 5-amino-3-(4-methoxyphenyl)pyrazole in
the same manner as in Example 94.

MP:284°C.

Anal. Calcd. for: C₂₃H₂₁ClN₄O: C, 68.23; H, 5.23; N, 13.84.

Found: C, 68.17; H, 5.29; N, 13.86.

25 MS(EI): 404(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H, t, J=7.3Hz), 1.58-
1.63(2H, m), 2.32-2.38(2H, m), 3.70(3H, s), 5.56(1H, s),
6.81(2H, d, J=7.2Hz), 7.09-7.12(2H, m), 7.17(1H, dd, J=7.3Hz and
7.2Hz), 7.24-7.30(3H, m), 9.85(1H, brs), 12.46(1H, brs).

30 Example 2914-(2,1,3-Benzoxadiazol-4-yl)-6-(2-bromothiophen-5-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 5-

bromothiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:208°C.

Anal. Calcd. for: C₁₇H₉BrN₆OS: C, 48.01; H, 2.13; N, 19.76.

5 Found: C, 47.94; H, 2.36; N, 19.78.

MS(EI): 425(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.54(1H, s), 7.32-7.34(2H, m), 7.42(1H, d, J=3.9Hz), 7.50(1H, d, J=6.6Hz), 7.61(1H, dd, J=9.0Hz), 7.95(1H, d, J=9.0Hz), 10.32(1H, brs), 12.32(1H, brs).

10 **Example 292**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(3-methylthiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3-methylthiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:202°C.

Anal. Calcd. for: C₁₈H₁₂N₆OS: C, 59.99; H, 3.36; N, 23.32.

Found: C, 59.89; H, 3.53; N, 23.06.

MS(EI): 360(M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.17(3H, s), 5.54(1H, s), 6.96(1H, d, J=5.1Hz), 7.32(1H, s), 7.49(1H, d, J=6.6Hz), 7.60-7.64(2H, m), 7.96(1H, d, J=9.0Hz), 10.19(1H, brs), 12.25(1H, brs).

Example 293

25 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methoxymethylindol-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 1-methoxymethylindol-3-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

30 MP:200°C.

MS(EI): 423(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.19(3H, s), 5.55-5.63(3H, m), 7.15(1H, dd, J=7.3Hz and 7.2Hz), 7.25(1H, dd, J=7.3Hz and 7.2Hz),

7.34(1H,s), 7.54(1H,d,J=7.3Hz), 7.60-7.66(3H,m), 7.93-7.97(2H,m), 10.12(1H,brs), 12.22(1H,brs).

Example 294

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-3-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:256°C.

Anal. Calcd. for: C₂₀H₁₇ClN₄S: C, 63.07; H, 4.50; N, 14.71.

Found: C, 62.98; H, 4.52; N, 14.68.

MS(EI): 380(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.86(3H,t,J=7.3Hz), 1.56-1.62(2H,m), 2.31-2.36(2H,m), 5.46(1H,s), 7.00-7.24(5H,m), 7.36(1H,d,J=7.3Hz), 7.50(1H,d,J=4.9Hz), 9.95(1H,brs), 12.74(1H,brs).

Example 295

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(furan-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl furan-2-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:253°C.

Anal. Calcd. for: C₂₀H₁₇ClN₄O: C, 65.84; H, 4.70; N, 15.36.

Found: C, 65.81; H, 4.84; N, 15.49.

MS(EI): 364(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H,t,J=7.3Hz), 1.58-1.63(2H,m), 2.32-2.36(2H,m), 5.48(1H,s), 6.31(1H,d,J=3.2Hz), 6.45(1H,d,J=1.5Hz), 7.14-7.23(3H,m), 7.36(1H,d,J=7.3Hz), 7.59(1H,s), 9.93(1H,brs), 12.76(1H,brs).

Example 296

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 2-methoxybenzoate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:>270°C.

5 Anal. Calcd. for: C₂₃H₂₁ClN₄O: C, 68.23; H, 5.23; N, 13.84.

Found: C, 68.23; H, 5.31; N, 13.87.

MS(EI): 404(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90(3H, t, J=7.3Hz), 1.60-

1.65(2H, m), 2.32-2.36(2H, m), 3.70(3H, s), 5.41(1H, s),

10 6.76(1H, dd, J=7.3Hz and 7.2Hz), 6.90-6.94(2H, m), 6.98-

7.04(2H, m), 7.08-7.15(2H, m), 7.22(1H, dd, J=7.3Hz and 7.2Hz),

9.83(1H, brs), 12.21(1H, brs).

Example 297

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(3-methoxyphenyl)-6-

15 propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3-methoxybenzoate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:239°C.

20 Anal. Calcd. for: C₂₃H₂₁ClN₄O: C, 68.23; H, 5.23; N, 13.84.

Found: C, 68.16; H, 5.31; N, 13.80.

MS(EI): 404(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H, t, J=7.3Hz), 1.58-

1.63(2H, m), 2.31-2.36(2H, m), 3.68(3H, s), 6.78(1H, d, J=7.3Hz),

25 6.87-6.89(2H, m), 7.11-7.20(4H, m), 7.29(1H, d, J=7.3Hz),

9.92(1H, brs), 12.64(1H, brs).

Example 298

4-(2,1,3-Benzoxadiazol-4-yl)-6-(2-chlorothiophen-5-yl)-5-
cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl 5-chlorothiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:210°C.

Anal. Calcd. for: $C_{17}H_9ClN_6OS$: C, 53.62; H, 2.38; N, 22.07.

Found: C, 53.51; H, 2.67; N, 22.13.

MS(EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54(1H, s), 7.23(1H, d, J=3.9Hz),
5 7.33(1H, s), 7.46(1H, d, J=3.9Hz), 7.50(1H, d, J=6.6Hz),
7.60(1H, dd, J=9.0Hz and 6.6Hz), 7.95(1H, d, J=9.0Hz),
10.31(1H, brs), 12.30(1H, brs).

Example 299

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-
10 methylthiophen-5-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 5-methylthiophene-2-carboxylate, 2,1,3-benzoxadiazol-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 192°C.

15 MS(EI): 360 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.50(3H, s), 5.52(1H, s),
6.87(1H, d, J=3.6Hz), 7.32(1H, s), 7.40(1H, d, J=3.7Hz),
7.48(1H, d, J=6.6Hz), 7.61(1H, dd, J=9.0Hz and 6.6Hz),
7.95(1H, d, J=9.0Hz), 10.12(1H, brs), 12.26(1H, brs).

20 Example 300

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(naphthalen-1-yl)-6-
propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl naphthalene-1-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the
25 same manner as in Example 290.

MP: 254°C.

Anal. Calcd. for: $C_{26}H_{21}ClN_4$: C, 73.49; H, 4.98; N, 13.19.

Found: C, 73.81; H, 5.05; N, 13.08.

MS(EI): 424 (M^+).

30 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, J=7.3Hz), 1.64-
1.70(2H, m), 2.46-2.49(2H, m), 5.25(1H, s), 6.88-7.02(5H, m),
7.31(1H, dd, J=7.3Hz and 7.2Hz), 7.42-7.47(3H, m), 7.83-
7.88(2H, m), 9.95(1H, brs), 12.46(1H, brs).

Example 3014-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(naphthalen-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl naphthalene-
5 2-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP: >270°C.

Anal. Calcd. for: C₂₆H₂₁ClN₄: C, 73.49; H, 4.98; N, 13.19.

Found: C, 73.23; H, 5.01; N, 13.26.

10 MS(EI): 424(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.91(3H, t, J=7.3Hz), 1.61-
1.66(2H, m), 2.31-2.41(2H, m), 5.76(1H, s), 7.05(1H, dd, J=7.3Hz
and 7.2Hz), 7.12-7.16(2H, m), 7.28(1H, d, J=7.3Hz), 7.45-
7.52(2H, m), 7.57(1H, d, J=7.3Hz), 7.77-7.84(4H, m), 9.94(1H, brs),
15 12.79(1H, brs).

Example 3024-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3,6-dipropyl-2H-pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (4.8 g) in THF (150 mL)
20 was added n-BuLi (67 mmol) at -78°C. Methyl butyrate (10 g) was added and the mixture was stirred for 1 hour. The reaction mixture was acidified with hydrochloric acid and extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column
25 chromatography (eluent: hexane-ethyl acetate (10:1)) to give 1-cyanopentan-2-one (5.5 g) as a colorless oil. To a solution of the obtained colorless oil in toluene was added hydrazine monohydrate (5.0 g) and the mixture was heated under reflux for 3 hours. The mixture was cooled and the solvent was
30 evaporated under reduced pressure. The reaction mixture was purified by silica gel column chromatography (eluent: chloroform-methanol (10:1)) to give 5-amino-3-propylpyrazole (5.0 g). A solution of 2-chloroaldehyde (1.7 g), 5-amino-3-

propylpyrazole (1.5 g) and 1-cyanopentan-2-one (1.6 g) in acetonitrile (20 mL) was heated under reflux overnight. The mixture was cooled to room temperature and the precipitated crystals were collected by filtration to give the title
5 compound (2.1 g) as colorless crystals.

MP:237°C.

Anal. Calcd. for: $C_{19}H_{21}ClN_4$: C, 66.95; H, 6.21; N, 16.44.

Found: C, 66.98; H, 6.26; N, 16.41.

MS(EI): 340 (M^+).

10 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.57(3H, t, J=7.3Hz),
0.91(3H, t, J=7.3Hz), 1.02-1.07(2H, m), 1.59-1.65(2H, m), 2.01-
2.12(2H, m), 2.30-2.38(2H, m), 5.28(1H, s), 7.20-7.23(2H, m),
7.30(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz),
9.70(1H, brs), 11.85(1H, brs).

15 **Example 303**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-hydroxy-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 2-chlorobenzaldehyde and 3-amino-5-hydroxypyrazole in the same
20 manner as in Example 94.

MS(EI): 314 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=7.3Hz), 1.56-
1.60(2H, m), 2.26-2.38(2H, m), 5.11(1H, s), 7.14-7.21(3H, m),
7.27(1H, dd, J=7.3Hz and 7.2Hz), 7.34(1H, d, J=7.3Hz),
25 9.64(1H, brs), 10.45(1H, brs).

Example 304

3-Butyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pentanoate,
30 methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:212°C.

Anal. Calcd. for: $C_{20}H_{23}ClN_4$: C, 67.69; H, 6.53; N, 15.79.

Found: C, 67.58; H, 6.46; N, 15.75.

MS(EI): 354(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.64(3H, t, J=7.3Hz), 0.89-
0.98(6H, m), 1.10-1.14(1H, m), 1.59-1.64(2H, m), 2.05-2.16(2H, m),
5 2.31-2.35(2H, m), 5.28(1H, s), 7.20-7.24(2H, m),
7.29(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz),
9.70(1H, brs), 11.85(1H, brs).

Example 305

4-(2,1,3-Benzoxadiazol-4-yl)-6-(benzothiophen-2-yl)-5-cyano-
10 4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
benzothiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde
and 3-aminopyrazole in the same manner as in Example 95.

MP: 220°C.

15 Anal. Calcd. for: C₂₁H₁₂N₆OS: C, 63.62; H, 3.05; N, 21.20.

Found: C, 63.58; H, 3.29; N, 21.09.

MS(EI): 396(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.60(1H, s), 7.36(1H, s), 7.44-
7.46(2H, m), 7.54(1H, d, J=6.3Hz), 7.64(1H, dd, J=9.0Hz and 6.6Hz),
20 7.88(1H, s), 7.94-7.98(2H, m), 8.05(1H, d, J=9.0Hz), 10.40(1H, brs),
12.31(1H, brs).

Example 306

4-(2-Chlorophenyl)-5-cyano-6-cyclohexyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl
cyclohexanecarboxylate, 2-chlorobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP: 163°C.

Anal. Calcd. for: C₁₉H₁₉ClN₄ 1/2 H₂O: C, 65.61; H, 5.80; N, 16.11.

30 Found: C, 65.40; H, 5.77; N, 15.86.

MS(EI): 338(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.16-1.30(3H, m), 1.66-1.85(7H, m),
2.66-2.72(1H, m), 5.33(1H, s), 7.21-7.25(3H, m),

7.32(1H,dd,J=7.3Hz and 7.2Hz), 7.41(1H,d,J=7.3Hz),
9.60(1H,brs), 12.15(1H,brs).

Example 307

6-t-Butyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo
5 [3,4-b]pyridine

The title compound was prepared from methyl pivalate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:198°C.

10 Anal. Calcd. for: C₁₇H₁₇ClN₄: C, 65.28; H, 5.48; N, 17.91.

Found: C, 64.98; H, 5.47; N, 17.78.

MS(EI): 312(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.41(9H,s), 5.33(1H,s), 7.21-
7.33(4H,m), 7.41(1H,d,J=7.3Hz), 8.88(1H,brs), 12.20(1H,brs).

15 Example 308

4-(2-Chlorophenyl)-5-cyano-3-cyclopropyl-4,7-dihydro-6-propyl-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
cyclopropanecarboxylate, methyl butyrate and 2-
20 chlorobenzaldehyde in the same manner as in Example 302.

MP:270°C.

Anal. Calcd. for: C₁₉H₁₉ClN₄: C, 67.35; H, 5.65; N, 16.54.

Found: C, 67.34; H, 5.66; N, 16.62.

MS(EI): 338(M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.22-0.25(1H,m), 0.41-0.44(1H,m),
0.50-0.54(1H,m), 0.62-0.66(1H,m), 0.90(3H,t,J=7.3Hz), 1.25-
1.29(1H,m), 1.58-1.63(2H,m), 2.31-2.36(2H,m), 5.33(1H,s), 7.18-
7.23(2H,m), 7.30(1H,dd,J=7.3Hz and 7.2Hz), 7.38(1H,d,J=7.3Hz),
9.69(1H,brs), 11.73(1H,brs).

30 Example 309

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-ethyl-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate,

methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:269°C.

Anal. Calcd. for: C₁₈H₁₉ClN₄: C, 66.15; H, 5.86; N, 17.14.

5 Found: C, 66.27; H, 5.86; N, 17.25.

MS(EI): 326(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.72(3H, t, J=7.3Hz),
0.91(3H, t, J=7.3Hz), 1.59-1.64(2H, m), 2.09-2.11(2H, m), 2.31-
2.40(2H, m), 5.29(1H, s), 7.20-7.24(2H, m), 7.30(1H, dd, J=7.3Hz
10 and 7.2Hz), 7.38(1H, d, J=7.3Hz), 9.70(1H, brs), 11.86(1H, brs).

Example 310

3-t-Butyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pivalate,
15 methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:>270°C.

Anal. Calcd. for: C₂₀H₂₃ClN₄: C, 67.69; H, 6.53; N, 15.79.

Found: C, 67.55; H, 6.56; N, 15.66.

20 MS(EI): 354(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.3Hz), 0.95(9H, s),
1.53-1.59(2H, m), 2.26-2.30(2H, m), 5.39(1H, s),
6.97(1H, d, J=7.3Hz), 7.20(1H, dd, J=7.3Hz and 7.2Hz),
7.27(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz),
25 9.73(1H, brs), 11.87(1H, brs).

Example 311

4-(2-Chlorophenyl)-5-cyano-3-cyclohexyl-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
30 cyclohexanecarboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:>270°C.

Anal. Calcd. for: C₂₂H₂₅ClN₄: C, 69.37; H, 6.62; N, 14.71.

Found: C, 69.17; H, 6.62; N, 14.91.

MS(EI): 380(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89-1.17(9H, m), 1.47-1.64(6H, m),
2.06-2.08(1H, m), 2.31-2.38(2H, m), 5.30(1H, s), 7.19-7.23(2H, m),
5 7.29(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz),
9.71(1H, brs), 11.83(1H, brs).

Example 312

4-(2-Chlorophenyl)-5-cyano-6-cycloheptyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl
cycloheptanecarboxylate, 2-chlorobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP: 146°C.

MS(EI): 352(M⁺).

15 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.42-1.98(12H, m), 2.78-
2.81(1H, m), 5.33(1H, s), 7.21-7.24(3H, m), 7.32(1H, dd, J=7.3Hz
and 7.2Hz), 7.41(1H, d, J=7.3Hz), 9.61(1H, brs), 12.18(1H, brs).

Example 313

4-(2-Chlorophenyl)-5-cyano-6-cyclobutyl-4,7-dihydro-2H-
20 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
cyclobutanecarboxylate, 2-chlorobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP: 188°C.

25 Anal. Calcd. for: C₁₇H₁₅ClN₄: C, 65.70; H, 4.86; N, 18.03.

Found: C, 65.51; H, 5.21; N, 18.27.

MS(EI): 310(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.72-1.77(1H, m), 1.93-1.97(1H, m),
2.09-2.12(2H, m), 2.38-2.43(2H, m), 2.58-2.61(1H, m), 5.33(1H, s),
30 7.20-7.32(4H, m), 7.41(1H, d, J=7.3Hz), 9.72(1H, brs),
12.18(1H, brs).

Example 314

4-(2-Chlorophenyl)-5-cyano-3-cyclopentyl-4,7-dihydro-6-propyl-

2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopentanecarboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

5 MP:>270°C.

Anal. Calcd. for: C₂₁H₂₃ClN₄: C, 68.75; H, 6.32; N, 15.27.

Found: C, 68.56; H, 6.36; N, 15.22.

MS(EI): 366(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H, t, J=7.3Hz), 1.31-
10 1.74(10H, m), 2.30-2.37(2H, m), 2.52-2.54(1H, m),
5.30(1H, s), 7.17-7.22(2H, m), 7.28(1H, dd, J=7.3Hz and 7.2Hz),
7.37(1H, d, J=7.3Hz), 9.71(1H, brs), 11.86(1H, brs).

Example 315

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-3-isopropyl-

15 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 2-methylpropionate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:>270°C.

20 Anal. Calcd. for: C₁₉H₂₁ClN₄: C, 66.95; H, 6.21; N, 16.44.

Found: C, 66.90; H, 6.27; N, 16.44.

MS(EI): 340(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.67(3H, d, J=7.2Hz),
0.90(3H, t, J=7.3Hz), 0.95(3H, d, J=7.3Hz), 1.57-1.63(2H, m), 2.30-
25 2.35(2H, m), 5.30(1H, s), 7.19-7.23(2H, m), 7.29(1H, dd, J=7.3Hz
and 7.2Hz), 7.38(1H, d, J=7.3Hz), 9.71(1H, brs), 11.88(1H, brs).

Example 316

4-(2-Chlorophenyl)-5-cyano-6-cyclopentyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl cyclopentanecarboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:225°C.

Anal. Calcd. for: $C_{18}H_{17}ClN_4 \cdot 1/5 H_2O$: C, 65.83; H, 5.34; N, 17.06.

Found: C, 66.02; H, 5.51; N, 16.62.

MS(EI): 324 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.56-1.60(2H, m), 1.78-1.87(6H, m),
5 3.06-3.10(1H, m), 5.34(1H, s), 7.22-7.26(3H, m),
7.32(1H, dd, $J=7.3$ Hz and 7.2Hz), 7.42(1H, d, $J=7.3$ Hz),
9.61(1H, brs), 12.16(1H, brs).

Example 317

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclopentyl-4,7-dihydro-
10 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopentanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 247°C.

15 MS(EI): 394 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.52-1.58(2H, m), 1.75-1.82(6H, m),
3.01-3.06(1H, m), 5.46(1H, s), 7.33(1H, s), 7.54-7.58(2H, m),
7.84(1H, d, $J=7.3$ Hz), 9.73(1H, brs), 12.25(1H, brs).

Example 318

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclopentyl-4,7-
20 dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopentanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

25 MP: 193°C.

Anal. Calcd. for: $C_{18}H_{16}N_6O$: C, 65.05; H, 4.85; N, 25.29.

Found: C, 64.72; H, 4.98; N, 24.86.

MS(EI): 332 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.55-1.58(2H, m), 1.80-1.86(6H, m),
30 3.06-3.09(1H, m), 5.39(1H, s), 7.26(1H, s), 7.38(1H, d, $J=6.6$ Hz),
7.60(1H, dd, $J=9.0$ Hz and 6.6Hz), 7.91(1H, d, $J=9.0$ Hz),
9.72(1H, brs), 12.15(1H, brs).

Example 319

4-(2-Bromo-3-cyanophenyl)-6-t-butyl-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pivalate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:251°C.

Anal. Calcd. for: $C_{18}H_{16}BrN_5 \cdot 1/2 H_2O$: C, 55.25; H, 4.38; N, 17.90.

Found: C, 55.55; H, 4.30; N, 18.14.

10 MS(EI): 382(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.41(9H, s), 5.46(1H, s), 7.33(1H, s), 7.54-7.60(2H, m), 7.82(1H, d, J=7.3Hz), 9.00(1H, brs), 12.29(1H, brs).

Example 320

15 4-(2,1,3-Benzoxadiazol-4-yl)-6-t-butyl-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pivalate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

20 MP:204°C.

Anal. Calcd. for: $C_{17}H_{16}N_6O \cdot 1/2 H_2O$: C, 63.03; H, 5.10; N, 25.94.

Found: C, 63.08; H, 5.08; N, 26.00.

MS(EI): 320(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.40(9H, s), 5.37(1H, s), 7.26(1H, s), 7.38(1H, d, J=6.6Hz), 7.59(1H, dd, J=9.0Hz and 6.6Hz), 7.91(1H, d, J=9.0Hz), 9.02(1H, brs), 12.20(1H, brs).

Example 321

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclobutyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl cyclobutanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:278°C.

Anal. Calcd. for: $C_{18}H_{14}BrN_5$: C, 56.86; H, 3.71; N, 18.42.

Found: C, 56.57; H, 3.79; N, 18.48.

MS(EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.71(1H, m), 1.88-1.95(1H, m),
5 2.06-2.13(2H, m), 2.38-2.47(2H, m), 3.56-3.60(1H, m), 5.45(1H, s),
7.33(1H, s), 7.57-7.59(2H, m), 7.82(1H, d, J=7.3Hz), 9.84(1H, brs),
12.27(1H, brs).

Example 322

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclobutyl-4,7-dihydro-
10 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclobutanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 194°C.

15 Anal. Calcd. for: $C_{17}H_{14}N_6O$: C, 64.14; H, 4.43; N, 26.40.

Found: C, 64.08; H, 4.51; N, 26.26.

MS(EI): 318 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.72-1.76(1H, m), 1.90-1.97(1H, m),
2.10-2.14(2H, m), 2.39-2.46(2H, m), 3.56-3.60(1H, m), 5.38(1H, s),
20 7.26(1H, s), 7.37(1H, d, J=6.6Hz), 7.58(1H, dd, J=9.0Hz and 6.6Hz),
7.91(1H, d, J=9.0Hz), 9.82(1H, brs), 12.17(1H, brs).

Example 323

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclohexyl-4,7-dihydro-
2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl cyclohexanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 210°C.

Anal. Calcd. for: $C_{19}H_{18}N_6O$: C, 65.88; H, 5.24; N, 24.26.

30 Found: C, 65.88; H, 5.25; N, 24.19.

MS(EI): 346 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.21-1.26(3H, m), 1.62-1.80(7H, m),
2.66-2.70(1H, m), 5.38(1H, s), 7.25(1H, s), 7.38(1H, d, J=6.6Hz),

7.59(1H,dd,J=9.0Hz and 6.6Hz), 7.91(1H,d,J=9.0Hz),
9.72(1H,brs), 12.15(1H,brs).

Example 324

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cycloheptyl-4,7-
5 dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
cycloheptanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and
3-aminopyrazole in the same manner as in Example 94.

MP:228°C.

10 Anal. Calcd. for: C₂₀H₂₀N₆O: C, 66.65; H, 5.59; N, 23.32.

Found: C, 66.45; H, 5.70; N, 22.97.

MS(EI): 360(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.38-1.98(12H,m), 2.76-
2.79(1H,m), 5.37(1H,s), 7.24(1H,s), 7.38(1H,d,J=6.6Hz),
15 7.58(1H,dd,J=9.0Hz and 6.6Hz), 7.91(1H,d,J=9.0Hz), 9.72(1H,brs),
12.13(1H,brs).

Example 325

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclohexyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl
cyclohexanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP:193°C.

Anal. Calcd. for: C₂₀H₁₈BrN₅ 1/2 H₂O: C, 57.56; H, 4.59; N, 16.78.

25 Found: C, 57.25; H, 4.37; N, 16.56.

MS(EI): 408(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21-1.26(3H,m), 1.66-1.80(7H,m),
2.66-2.69(1H,m), 5.45(1H,s), 7.33(1H,s), 7.55-7.60(2H,m),
7.82(1H,d,J=7.3Hz), 9.73(1H,brs), 12.24(1H,brs).

Example 326

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cycloheptyl-4,7-dihydro-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl

cycloheptanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:252°C.

Anal. Calcd. for: $C_{21}H_{20}BrN_5 \cdot 1/2 H_2O$: C, 58.48; H, 4.91; N, 16.24.

5 Found: C, 58.53; H, 4.73; N, 16.19.

MS(EI): 422 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.44-1.58(12H, m), 2.76-2.79(1H, m), 5.44(1H, s), 7.31(1H, s), 7.54-7.60(2H, m), 7.83(1H, d, $J=7.3$ Hz), 9.73(1H, brs), 12.23(1H, brs).

10 **Example 327**

5-Cyano-4,7-dihydro-6-propyl-4-(pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, pyridine-3-aldehyde and 3-aminopyrazole in the same manner as
15 in Example 94.

MP:201°C.

Anal. Calcd. for: $C_{15}H_{15}N_5$: C, 67.90; H, 5.70; N, 26.40.

Found: C, 67.42; H, 5.74; N, 26.72.

MS(EI): 265 (M^+).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, $J=7.3$ Hz), 1.62-1.67(2H, m), 2.36-2.39(2H, m), 4.98(1H, s), 7.27(1H, s), 7.35(1H, dd, $J=7.3$ Hz and 2.9Hz), 7.54(1H, d, $J=7.3$ Hz), 8.41-8.44(2H, m), 9.81(1H, brs), 12.18(1H, brs).

Example 328

25 3-t-Butoxycarbonyloxy-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine

To a solution of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-3-hydroxy-6-propyl-2H-pyrazolo[3,4-b]pyridine (12.5 g) in THF (400 mL) was added triethylamine (4.5 g),
30 dimethylaminopyridine (0.5 g) and di-t-butylcarbonate (9.6 g) and the mixture was stirred for 3 hours. The mixture was extracted with ethyl acetate and the solvent was evaporated under reduced pressure. The residue was recrystallized from

ethyl acetate to give the title compound (12 g) as colorless crystals.

MP:182°C.

Anal. Calcd. for: $C_{21}H_{23}ClN_4O_3$: C, 60.79; H, 5.59; N, 13.50.

5 Found: C, 60.60; H, 5.50; N, 13.44.

MS(EI): 414 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, J=7.3Hz), 1.54(9H, s),
2.49-2.51(2H, m), 5.18(1H, s), 7.23-7.27(2H, m),
7.32(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz),
10 9.15(1H, brs), 10.99(1H, brs).

Example 329

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(2,2-dimethoxyethyl)-
4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3,3-
15 dimethoxypropionate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:115°C.

Anal. Calcd. for: $C_{17}H_{16}N_6O_3 \cdot 1.0 H_2O$: C, 55.13; H, 4.90; N, 22.69.

Found: C, 55.30; H, 4.51; N, 22.99.

20 MS(EI): 352 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.71(2.75(2H, m), 3.28(3H, s),
3.31(3H, s), 4.74(1H, t, J=5.9Hz), 5.43(1H, s), 7.28(1H, s),
7.40(1H, d, J=6.6Hz), 7.61(1H, dd, J=9.0Hz and 6.6Hz),
7.92(1H, d, J=9.0Hz), 9.99(1H, brs), 12.18(1H, brs).

25 Example 330

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(2,2-dimethoxyethyl)-
6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3,3-
dimethoxypropionate, methyl butyrate and 2-chlorobenzaldehyde
30 in the same manner as in Example 302.

MP:180°C.

Anal. Calcd. for: $C_{20}H_{23}ClN_4O_2$: C, 62.09; H, 5.99; N, 14.48.

Found: C, 62.35; H, 6.02; N, 14.50.

MS(EI):386(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.91(3H,t,J=7.3Hz), 1.59-
1.64(2H,m), 2.28-2.35(4H,m), 3.00(3H,s), 3.02(3H,s),
3.81(1H,t,J=7.3Hz), 5.31(1H,s), 7.24-7.31(3H,m),
5 7.40(1H,d,J=7.3Hz), 9.75(1H,brs), 11.92(1H,brs).

Example 331

4-(2,1-Benzoisoxazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate,
10 2,1-benzoisoxazole-4.aldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:239°C.

MS(EI):305(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.91(3H,t,J=7.3Hz), 1.64-
15 1.67(2H,m), 2.40-2.43(2H,m), 5.23(1H,s), 6.91(1H,d,J=6.6Hz),
7.28(1H,s), 7.36(1H,dd,J=9.3Hz and 6.6Hz), 7.52(1H,d,J=9.3Hz),
9.37(1H,s), 9.96(1H,brs), 12.21(1H,brs).

Example 332

4-(2,1-Benzoisoxazol-4-yl)-5-cyano-4,7-dihydro-6-isopropyl-2H-
20 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
2,1-benzoisoxazole-4.aldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:245°C.

25 MS(EI):305(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 1.23-1.26(6H,m),
3.03(1H,t,J=5.9Hz), 5.21(1H,s), 6.92(1H,d,J=6.6Hz), 7.30(1H,s),
7.37(1H,dd,J=9.3Hz and 6.6Hz), 7.53(1H,d,J=9.3Hz), 9.34(1H,s),
9.78(1H,brs), 12.23(1H,brs).

30 **Example 333**

4-(2,1-Benzoisoxazol-4-yl)-5-cyano-6-cyclopropyl-4,7-dihydro-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl

cyclopropanecarboxylate, 2,1-benzisoxazole-4.aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:248°C.

MS(EI):303(M⁺).

5 ¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.89-0.91(2H,m), 1.05-1.08(2H,m), 1.94-1.98(2H,m), 5.20(1H,s), 6.91(1H,d,J=6.6Hz),7.28(1H,s), 7.36(1H,dd,J=9.3Hz and 6.6Hz), 7.52(1H,d,J=9.3Hz), 9.26(1H,s), 9.36(1H,brs),12.22(1H,brs).

Example 334

10 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(1-t-butoxycarbonylindol-3-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 1-t-butoxycarbonylindole-3-carboxylate, 2,1,3-benzoxadiazole-4-
15 aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:202°C.

MS(EI):479(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 1.65(9H,s), 5.60(1H,s), 7.27-
20 7.41(3H,m), 7.54-7.58(2H,m), 7.64(1H,dd,J=7.3Hz and 7.2Hz), 7.97(1H,d,J=7.3Hz), 8.03(1H,s), 8.10(1H,d,J=7.3Hz), 10.23(1H,brs), 12.26(1H,brs).

Example 335

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(indol-3-yl)-2H-pyrazolo[3,4-b]pyridine
25

(1-t-Butoxycarbonylindol-3-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (0.6 g) was added to trifluoroacetic acid (15 mL) under ice-cooling and the mixture was stirred for 3 hours. The solvent was evaporated under reduced pressure,
30 and ethyl acetate and a saturated aqueous sodium hydrogencarbonate solution were added to neutralize the mixture. The mixture was extracted with ethyl acetate and the solvent was evaporated under reduced pressure. The residue was

recrystallized from ethyl acetate to give the title compound (0.4 g) as colorless crystals.

MP:238°C.

Anal. Calcd. for: $C_{21}H_{13}N_7O \cdot 3/5 H_2O$: C, 64.64; H, 3.67; N, 25.13.

5 Found: C, 64.77; H, 4.05; N, 25.59.

MS(EI): 379 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.56(1H, s), 7.08(1H, dd, J=7.3Hz and 7.2Hz), 7.15(1H, dd, J=7.3Hz and 7.2Hz), 7.44(1H, s), 7.44-7.54(3H, m), 7.65(1H, dd, J=7.3Hz and 7.2Hz), 7.76(1H, s),
10 7.95(1H, d, J=7.3Hz), 9.98(1H, brs), 11.63(1H, brs), 12.20(1H, brs).

Example 336

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-dimethoxymethyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
15 dimethylacetate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:212°C.

Anal. Calcd. for: $C_{19}H_{21}ClN_4O_2$: C, 61.21; H, 5.68; N, 15.03.

Found: C, 61.25; H, 5.69; N, 15.17.

20 MS(EI): 372 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, J=7.3Hz), 1.57-1.63(2H, m), 2.28-2.35(2H, m), 2.93(6H, s), 4.93(1H, s), 5.30(1H, s), 7.10(1H, d, J=7.3Hz), 7.19(1H, dd, J=7.3Hz and 7.2Hz), 7.25(1H, dd, J=7.3Hz and 7.2Hz), 7.35(1H, d, J=7.3Hz),
25 9.80(1H, brs), 12.29(1H, brs).

Example 337

5-Cyano-4,7-dihydro-6-propyl-4-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate,
30 pyridine-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:224°C.

Anal. Calcd. for: $C_{15}H_{15}N_5$: C, 67.90; H, 5.70; N, 26.40.

Found: C, 67.90; H, 5.79; N, 26.31.

MS(EI): 265(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.92(3H, t, J=7.3Hz), 1.62-
1.67(2H, m), 2.35-2.43(2H, m), 4.95(1H, s), 7.20(2H, dd, J=4.6Hz
5 and 1.5Hz), 7.29(1H, s), 8.50(2H, dd, J=4.6Hz and 1.5Hz),
9.84(1H, brs), 12.20(1H, brs).

Example 338

5-Cyano-4,7-dihydro-4-(3-methyl-2-nitrophenyl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl butyrate, 3-
methyl-2-nitrobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: 250°C.

Anal. Calcd. for: C₁₇H₁₇N₅O₂: C, 63.15; H, 5.30; N, 21.66.

15 Found: C, 62.89; H, 5.51; N, 22.11.

MS(EI): 323(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.63-
1.68(2H, m), 2.26(3H, s), 2.36-2.42(2H, m), 4.83(1H, s),
7.17(1H, s), 7.20(1H, d, J=7.3Hz), 7.32(1H, d, J=7.3Hz),
20 7.48(1H, dd, J=7.3Hz and 7.2Hz), 9.91(1H, brs), 12.22(1H, brs).

Example 339

5-Cyano-4,7-dihydro-4-(3-methyl-2-nitrophenyl)-6-isopropyl-2H-
pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl isobutyrate,
3-methyl-2-nitrobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: 261°C.

Anal. Calcd. for: C₁₇H₁₇N₅O₂ 1/2 H₂O: C, 61.43; H, 5.46; N, 21.07.

Found: C, 61.82; H, 5.32; N, 21.31.

30 MS(EI): 323(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, d, J=7.2Hz),
1.26(3H, d, J=7.2Hz), 2.25(3H, s), 3.01(1H, t, J=7.2Hz), 4.84(1H, s),
7.17(1H, s), 7.22(1H, d, J=7.3Hz), 7.32(1H, d, J=7.3Hz),

7.48(1H,dd,J=7.3Hz and 7.2Hz), 9.71(1H,brs), 12.24(1H,brs).

Example 340

5-Cyano-6-cyclopropyl-4,7-dihydro-4-(3-methyl-2-nitrophenyl)-
2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl
cyclopropanecarboxylate, 3-methyl-2-nitrobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP:265°C.

Anal. Calcd. for: C₁₇H₁₅N₅O₂: C, 63.54; H, 4.71; N, 21.79.

10 Found: C, 63.44; H, 4.85; N, 22.04.

MS(EI): 321(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-1.07(4H,m), 1.96-
1.99(1H,m), 2.26(3H,s), 4.81(1H,s), 7.17(1H,s),
7.20(1H,d,J=7.3Hz), 7.32(1H,d,J=7.3Hz), 7.48(1H,dd,J=7.3Hz and
15 7.2Hz), 9.23(1H,brs), 12.23(1H,brs).

Example 341

Ethyl 4-(2,1,3-benzoxazol-4-yl)-4,7-dihydro-6-(1-methylethyl)-
2H-pyrazolo[3,4-b]pyridine-5-carboxylate 1/2 ethyl acetate

20 The title compound was prepared from 2,1,3-benzoxazole-
4-aldehyde, 3-aminopyrazole and ethyl isobutyrylacetate in the
same manner as in Example 275.

MP:190-193°C (decomposition)

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.7.3(3H,t,J=7.1Hz),
1.19(3H,d,J=7.1Hz), 1.29(3H,d,J=7.1Hz), 3.77(2H,m), 4.37(1H,m),
25 5.69(1H,s), 7.12(1H,d,J=6.6Hz), 7.22(1H,s),
7.51(1H,dd,J=6.6,9.0Hz), 7.78(1H,d,J=8.8Hz), 9.31(1H,brs),
12.02(1H,brs).

Example 342

30 Ethyl 4-(2-nitrophenyl)-4,7-dihydro-6-(1-methylethyl)-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-nitrobenzaldehyde,
3-aminopyrazole and ethyl isobutyrylacetate in the same manner
as in Example 275.

MP:205-206°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.78(3H, t, J=6.8Hz),
1.15(3H, d, J=7.1Hz), 1.26(3H, d, J=7.1Hz), 3.71(2H, m), 4.33(1H, m),
5.44(1H, s), 7.29-7.34(3H, m), 7.58(1H, m), 7.78(1H, d, J=8.0Hz),
5 9.33(1H, brs), 12.11(1H, brs).

Example 343

Ethyl 4-(2-methoxyphenyl)-4,7-dihydro-6-(1-methylethyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate 1/2 ethyl acetate

The title compound was prepared from 2-
10 methoxybenzaldehyde, 3-aminopyrazole and ethyl isobutyrylacetate in the same manner as in Example 275.

MP:179-180°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.81(3H, t, J=7.1Hz),
1.17(3H, d, J=7.1Hz), 1.27(3H, d, J=7.1Hz), 3.76(2H, m), 3.85(3H, s),
15 4.31(1H, m), 5.46(1H, s), 6.77(1H, m), 6.89(1H, d, J=8.0Hz),
6.94(1H, d, J=7.6Hz), 7.04(1H, m), 7.14(1H, s), 8.98(1H, brs),
11.86(1H, brs).

Example 344

Ethyl 4-(2-bromophenyl)-4,7-dihydro-6-cyclopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from
cyclopropanecarbonyl chloride, 2-bromobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 277.

MP:168-170°C

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.86(3H, t, J=7.1Hz), 0.87-
0.90(2H, m), 1.10-1.14(2H, m), 3.16(1H, m), 3.78(2H, m),
5.57(1H, s), 7.01(1H, dd, J=5.8, 7.6Hz), 7.09(1H, d, J=7.8Hz),
7.24(1H, m), 7.29(1H, s), 7.51(1H, d, J=6.8Hz), 8.65(1H, brs),
12.01(1H, brs).

30 **Example 345**

Ethyl 4-(2-bromo3-cyanophenyl)-4,7-dihydro-6-cyclopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from

cyclopropanecarbonyl chloride, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 277.

MP:168-170°C

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.86(3H, t, J=7.1Hz), 0.88-
5 1.00(2H, m), 1.10-1.18(2H, m), 3.14(1H, m), 3.80(2H, m),
5.64(1H, s), 7.33(1H, s), 7.34-7.49(2H, m), 7.68(1H, m),
8.77(1H, brs), 12.10(1H, brs).

Example 346

4-(2-Chlorophenyl)-5-cyano-7-methyl-6-propyl-4,7-dihydro-2H-
10 pyrazolo[3,4-b]pyridine

A solution of 3-aminopyrazole (3.0 g), di-t-butyl dicarbonate (17.3 g) and dimethylaminopyridine (1.3 g) in tetrahydrofuran (360 ml) was stirred at room temperature. The reaction mixture was concentrated under reduced pressure. The
15 obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give a mixture (7.9 g) of 1-(t-butoxycarbonyl)-3-(t-butoxycarbonylamino)pyrazole and 2-(t-butoxycarbonyl)-3-(t-butoxycarbonylamino)pyrazole as a white amorphous solid. To a
20 suspension of the obtained white amorphous solid (7.9 g) and sodium hydride (1.1 g) in DMF (80 ml) was added methyl iodide (4.0 g) under ice-cooling and the mixture was stirred at room temperature for 1 hour. To the reaction mixture was added water under ice-cooling and the resulting mixture was
25 extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to
30 give a white solid (5.3 g). The obtained white solid (5.3 g) was dissolved in methylene chloride (50 ml), and trifluoroacetic acid (7 ml) was added. The resulting mixture was stirred at room temperature for 20 hours. The reaction

mixture was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: chloroform-methanol (10:1)) to give 3-methylaminopyrazole (1.54 g) as a colorless transparent oil.

- 5 Subsequently, the title compound was prepared from methyl butyrate, 2-chlorobenzaldehyde and 3-methylaminopyrazole in the same manner as in Example 94.

MP:170-171°C

Anal. Calcd. for: $C_{17}H_{17}N_4Cl$: C, 65.28; H, 5.48; N, 17.91.

- 10 Found: C, 65.14; H, 5.52; N, 17.72.

MS(EI): 312 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.00(3H, t, J=7.3Hz), 1.68(2H, m), 2.62(2H, m), 3.36(3H, s), 5.36(1H, s), 7.22-7.26(2H, m), 7.30-7.32(2H, m), 7.42(1H, d, J=8.1Hz), 12.31(1H, brs).

- 15 **Example 347**

4-(2,1,3-Benzoxazol-4-yl)-5-cyano-7-methyl-6-propyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

- The title compound was prepared from methyl butyrate, 2,1,3-benzoxazole-4-aldehyde and 3-methylaminopyrazole in the same manner as in Example 346.

MP:198-200°C

Anal. Calcd. for: $C_{17}H_{16}N_6O$: C, 63.74; H, 5.03; N, 26.23.

Found: C, 63.78; H, 5.12; N, 26.47.

MS(EI): 320 (M^+).

- 25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.97(3H, t, J=7.4Hz), 1.61(2H, m), 2.63(2H, m), 3.41(3H, s), 5.40(1H, s), 7.32(1H, s), 7.40(1H, d, J=6.6Hz), 7.59(1H, dd, J=6.5, 6.6Hz), 7.92(1H, d, J=9.3Hz), 12.30(1H, brs).

Example 348

- 30 4-(2-Bromo-3-cyanophenyl)-5-cyano-7-methyl-6-propyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 2-bromo-3-cyanobenzaldehyde and 3-methylaminopyrazole in the

same manner as in Example 346.

MP:218-220°C

Anal. Calcd. for: C₁₈H₁₆N₅Br: C, 56.56; H, 4.22; N, 18.32.

Found: C, 56.60; H, 4.41; N, 18.18.

5 MS(EI): 382(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.00(3H, t, J=7.3Hz), 1.63(2H, m),
2.62(2H, m), 3.37(3H, s), 5.47(1H, s), 7.39(1H, s), 7.56-
7.58(2H, m), 7.83(1H, m), 12.41(1H, brs).

Example 349

10 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl acetate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

15 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.14(3H, s), 5.35(1H, s), 7.21-
7.33(4H, m), 7.42(1H, d, J=8.1Hz), 9.87(1H, brs), 12.15(1H, brs).

Example 350

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(morpholin-4-
yl)methyl-2H-pyrazolo[3,4-b]pyridine dihydrochloride

20 A solution of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine (22.9 g), di-t-butyl dicarbonate (19.4 g) and dimethylaminopyridine (0.5 g) in tetrahydrofuran (200 ml) was stirred at room temperature for 30 minutes. The reaction mixture was ice-cooled and the
25 precipitated crystals were collected by filtration to give 2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine (21.8 g) as white crystals.
2-(t-Butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine (5.0 g), N-bromosuccinimide
30 (2.5 g) and azobisisobutyronitrile (66 mg) were suspended in benzene (50 ml) and the suspension was stirred for 1 hour. The reaction mixture was concentrated under reduced pressure, and the obtained residue was purified by silica gel column

chromatography (eluent: hexane-ethyl acetate (2:1)) and crystallized from ethyl acetate to give 6-bromomethyl-2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine as white crystals. To a suspension of
5 sodium hydride (32 mg) in DMF (10 ml) was added morpholine (70 μ l) and the mixture was stirred at room temperature for 30 minutes. To the reaction mixture was added 6-bromomethyl-2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (0.36 g) and the mixture was stirred
10 under ice-cooling for 1 hour. To the reaction mixture was added water, and the precipitated crystals were collected by filtration and washed with hexane to give 2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-(morpholin-4-yl)methyl-2H-pyrazolo[3,4-b]pyridine (450 mg) as
15 white crystals. A solution of 2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-(morpholin-4-yl)methyl-2H-pyrazolo[3,4-b]pyridine (440 mg) in trifluoroacetic acid (5 ml) was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure and
20 4M hydrochloric acid-dioxane solution was added. The precipitated crystals were collected by filtration and washed with ethyl acetate to give the title compound (250 mg) as pale-yellow crystals.

MP:210-214°C (decomposition).

25 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 3.20-3.40(3H,m), 3.84-4.00(3H,m), 4.17-4.40(4H,m), 5.49(1H,s), 7.26-7.37(4H,s), 7.45(1H,d, J=7.8Hz), 10.22(1H,brs), 11.05(1H,brs), 12.33(1H,brs).

Example 351

30 6-Benzylloxymethyl-4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl benzyloxyacetate, 2-chlorobenzaldehyde and 3-aminopyrazole in

the same manner as in Example 94.

MP:165-166°C

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 4.35(2H, d, J=2.9Hz), 4.57(2H, s), 5.42(1H, s), 7.24-7.45(10H, m), 10.03(1H, brs), 12.22(1H, brs).

5 **Example 352**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(methylpiperazin-1-yl)methyl-2H-pyrazolo[3,4-b]pyridine dihydrochloride

4-(2-Chlorophenyl)-5-cyano-6-(t-butyldimethylsilyloxy)-methyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine was prepared
10 from ethyl t-butyldimethylsilyloxyacetate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94. To a solution of 4-(2-chlorophenyl)-5-cyano-6-(t-butyldimethylsilyloxy)methyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (10 g) in tetrahydrofuran (100 ml) was added a THF
15 solution (24.9 ml) of 1.0 M tetrabutylammonium fluoride and the mixture was stirred at room temperature for 1 hour. To the reaction mixture was added ethyl acetate (200 ml), and the resulting mixture was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate.
20 The solvent was evaporated and the obtained residue was crystallized from ethyl acetate to give 4-(2-chlorophenyl)-5-cyano-6-hydroxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (5.46 g) as a white solid. To a solution of 4-(2-chlorophenyl)-5-cyano-6-hydroxymethyl-4,7-dihydro-2H-
25 pyrazolo[3,4-b]pyridine (1.0 g) and carbon tetrabromide (1.27 g) in methylene chloride (35 ml) was added triphenylphosphine (1.0 g) under ice-cooling and the mixture was stirred under ice-cooling for 4 hours. The reaction mixture was concentrated under reduced pressure and the obtained residue was purified
30 by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (0.45 g) as a pale-yellow solid. To a suspension of sodium hydride (25 mg)

in DMF (3 ml) was added 1-methylpiperazine (69 μ l) and the mixture was stirred at room temperature for 30 minutes. To this reaction mixture was added a solution of 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (200 mg) in DMF (3 ml) under ice-cooling and the mixture was stirred under ice-cooling for 1 hour. To the reaction mixture was added water and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: ethyl acetate-methanol (4:1)). The obtained oil was treated with hydrogen chloride-methanol to give the title compound (87 mg) as white crystals.

MP:222-225°C (decomposition)

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 2.66-2.75(2H,m), 2.75(3H,s), 3.00-3.10(4H,m), 3.41-3.55(4H,m), 5.42(1H,s), 7.24-7.36(4H,m), 7.43(1H,d,J=8.0Hz), 9.77(1H,brs), 12.17(1H,brs).

Example 353

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(piperidin-1-yl)methyl-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine and piperidine in the same manner as in Example 352.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.43(1H,m), 1.67-1.82(5H,m), 3.05-3.25(2H,m), 3.48(2H,m), 4.10(2H,m), 5.49(1H,s), 7.26-7.35(4H,m), 7.45(1H,d,J=8.0Hz), 10.28(1H,brs), 10.59(1H,brs).

Example 354

Ethyl 4-(2-nitrophenyl)-4,7-dihydro-6-cyclopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from cyclopropanecarbonyl chloride, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 277.

MP:162-164°C (decomposition)

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.81(3H, t, J=7.4Hz), 0.85-
0.95(2H, m), 1.10-1.18(2H, m), 3.12(1H, m), 3.72(2H, m),
5.46(1H, s), 7.27-7.34(3H, m), 7.58(1H, m), 7.78(1H, d, J=8.0Hz),
5 8.78(1H, brs), 12.12(1H, brs).

Example 355

Ethyl 4-(2,1,3-benzoxazol-4-yl)-4,7-dihydro-6-cyclopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from
10 cyclopropanecarbonyl chloride, 2,1,3-benzoxazole-4-aldehyde
and 3-aminopyrazole in the same manner as in Example 277.

MP:109-111°C (decomposition).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.76(3H, t, J=6.8Hz), 0.85-
0.86(2H, m), 1.14-1.18(2H, m), 3.12(1H, m), 3.80(2H, m),
15 5.69(1H, s), 7.13(1H, d, J=6.6Hz), 7.23(1H, s), 7.51(1H, m),
7.79(1H, d, J=9.0Hz), 8.83(1H, brs), 12.05(1H, brs).

Example 356

4-(2,1,3-Benzoxazol-4-yl)-5-cyano-4,7-dihydro-2-(phenylcarbamoyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

20 The title compound was obtained as colorless crystals
from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and phenylisocyanate in the same manner as in Example 204.

MS(EI):425(M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.91(3H, t, J=7.3Hz), 1.64(2H, m),
2.58(2H, m), 5.44(1H, s), 7.10(1H, dd, J=6.3 and 7.6Hz), 7.31-
7.34(2H, m), 7.52(1H, d, J=6.6Hz), 7.59-7.64(3H, m), 7.95(1H, s),
7.97(1H, d, J=9.0Hz), 9.83(1H, brs), 10.30(1H, brs).

Example 357

30 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-1-(4-pentenoyl)-6-propyl-1H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-

pyrazolo[3,4-b]pyridine, dimethylaminopyridine and 4-pentenoyl chloride in the same manner as in Example 204.

MP:140°C.

Anal. Calcd. for: C₂₁H₂₁ClN₄O: C, 66.22; H, 5.62; N, 14.71.

5 Found: C, 66.20; H, 5.60; N, 14.65.

MS(EI): 380(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.95(3H, t, J=7.3Hz), 1.62(2H, m),
2.39-2.58(4H, m), 3.11(2H, t, J=7.6Hz), 4.98(1H, d, J=7.1Hz),
5.06(1H, d, J=10.3Hz), 5.40(1H, s), 5.85(1H, m), 7.27-7.37(4H, m),
10 7.46(1H, d, J=7.0Hz), 9.58(1H, brs).

Example 358

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-2-(4-pentenoyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
15 from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and 4-pentenoyl chloride in the same manner as in Example 204.

MP:176-177°C.

Anal. Calcd. for: C₂₁H₂₁ClN₄O: C, 66.22; H, 5.56; N, 14.71.

20 Found: C, 66.15; H, 5.63; N, 14.55.

MS(EI): 380(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.95(3H, t, J=7.3Hz), 1.67(2H, m),
2.34-2.49(4H, m), 3.00(2H, t, J=7.6Hz), 4.96(1H, d, J=10.6Hz),
5.02(1H, d, J=27.1Hz), 5.36(1H, s), 5.82(1H, m), 7.30-7.35(3H, m),
25 7.46(1H, d, J=7.8Hz), 7.83(1H, s), 10.39(1H, brs).

Example 359

5-Cyano-4,7-dihydro-4-(6-methylpyridin-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 6-
30 methylpyridine-2-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:177-181°C.

Anal. Calcd. for: C₁₆H₁₇N₅ 4/5 H₂O: C, 65.42; H, 6.38; N, 23.84.

Found: C, 65.52; H, 6.31; N, 24.19.

MS(EI): 279(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.95(3H, t, J=7.6Hz), 1.66(2H, m),
2.41(2H, m), 2.43(3H, s), 4.94(1H, s), 6.98(1H, d, J=7.6Hz),
5 7.06(1H, d, J=7.5Hz), 7.21(1H, s), 7.62(1H, dd, J=7.6 and 7.7Hz),
9.71(1H, brs), 12.09(1H, brs).

Example 360

4-(5-Cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-
b]pyridine)pyridine-N-oxide

10 The title compound was prepared from methyl butyrate,
pyridine-4-aldehyde-N-oxide and 3-aminopyrazole in the same
manner as in Example 94.

MP: 110-115°C.

Anal. Calcd. for: C₁₅H₁₅N₅O: C, 62.01; H, 6.18; N, 24.11.

15 Found: C, 61.94; H, 5.85; N, 23.73.

MS(EI): 283(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.91(3H, t, J=7.3Hz), 1.62(2H, m),
2.36(2H, m), 4.98(1H, s), 7.18(2H, d, J=6.6Hz), 7.31(1H, s),
8.14(2H, d, J=6.3Hz), 9.86(1H, brs), 12.2(1H, brs).

20 **Example 361**

5-Cyano-4,7-dihydro-4-(3-(4-morpholinomethyl)phenyl)-6-propyl-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 3-
(4-morpholinomethyl)benzaldehyde and 3-aminopyrazole in the
25 same manner as in Example 94.

MS(EI): 363(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.92(3H, t, J=7.3Hz), 1.63(2H, m),
2.30(4H, m), 2.30(2H, m), 3.40(2H, s), 3.53(4H, m), 4.86(1H, s),
7.05(1H, d, J=7.8Hz), 7.10(1H, d, J=7.6Hz), 7.14(1H, s), 7.19(1H, s),
30 7.23(1H, dd, J=7.5 and 7.6Hz), 9.70(1H, brs), 12.10(1H, brs).

Example 362

4-(3-Bromophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 3-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:202-205°C.

5 Anal. Calcd. for: $C_{16}H_{15}BrN_4$: C, 55.99; H, 4.41; N, 16.32.

Found: C, 55.82; H, 4.46; N, 17.03.

MS(EI): 343(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, J=7.3Hz), 1.63(2H, m),
2.37(2H, m), 4.92(1H, s), 7.18(1H, d, J=7.9Hz), 7.25(1H, s),
10 7.28(1H, d, J=7.8Hz), 7.33(1H, s), 7.39(1H, d, J=8.3Hz),
9.80(1H, brs), 12.18(1H, brs).

Example 363

5-Cyano-4,7-dihydro-4-(4-fluoro-2-chlorophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from methyl butyrate, 2-chloro-4-fluorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:209-212°C.

Anal. Calcd. for: $C_{16}H_{14}ClFN_4$: C, 60.67; H, 4.45; N, 17.69.

20 Found: C, 60.48; H, 4.48; N, 17.87.

MS(EI): 316(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.93(3H, t, J=7.3Hz), 1.64(2H, m),
2.39(2H, m), 5.33(1H, s), 7.17-7.40(3H, m), 7.41(1H, dd, J=2.7 and
6.1Hz), 9.85(1H, brs), 12.17(1H, brs).

25 Example 364

5-Cyano-4,7-dihydro-4-(3-(morpholin-4-yl)phenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 3-(morpholin-4-yl)benzaldehyde and 3-aminopyrazole in the same
30 manner as in Example 94.

MP:196-200°C.

Anal. Calcd. for: $C_{20}H_{23}N_5O$: C, 68.47; H, 6.63; N, 20.04.

Found: C, 68.41; H, 6.77; N, 20.16.

MS(EI):349(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.92(3H,t,J=7.3Hz), 1.63(2H,m),
2.32(2H,m), 3.05(4H,t,J=4.6Hz), 7.71(4H,t,J=4.6Hz), 4.80(1H,s),
6.59(1H,d,J=7.5Hz), 6.74(1H,m), 6.76(1H,s), 7.13(1H,dd,J=7.8
5 and 7.8Hz), 7.21(1H,s), 9.67(1H,brs), 12.02(1H,brs).

Example 365

5-Cyano-4,7-dihydro-4-(3-(morpholin-4-yl)phenyl)-6-isopropyl-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
10 3-(morpholin-4-yl)benzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:254-257°C.

Anal. Calcd. for:C₂₀H₂₃N₅O:C,68.47;H,6.63;N,20.04.

Found:C,68.56;H,6.73;N,20.30.

15 MS(EI):349(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 1.20(3H,d,J=7.0Hz),
1.22(3H,d,J=7.1Hz), 3.02(2H,m), 3.04(4H,t,J=4.8Hz),
3.70(4H,t,J=4.8Hz), 4.78(1H,s), 6.59(1H,d,J=7.6Hz), 7.74(1H,s),
7.13(1H,dd,J=7.5 and 8.1Hz), 7.22(1H,s), 9.48(1H,brs),
20 12.09(1H,brs).

Example 366

5-Cyano-6-cyclopropyl-4,7-dihydro-4-(3-(morpholin-4-
yl)phenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
25 cyclopropanecarboxylate, 3-(morpholin-4-yl)benzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

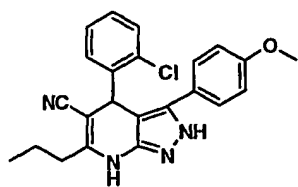
MP:>260°C.

MS(EI):347(M⁺).

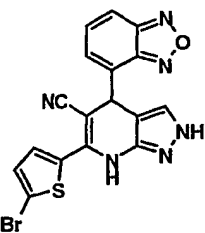
¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.86(4H,m), 1.93-1.98(1H,m),
30 3.05(4H,t,J=4.6Hz), 3.70(4H,t,J=4.6Hz), 4.79(1H,s),
6.56(1H,d,J=7.5Hz), 6.74(1H,s), 6.77(1H,s), 7.13(1H,dd,J=7.8
and 7.8Hz), 7.20(1H,s), 8.98(1H,brs),12.09(1H,brs).

The compounds of the above-described Examples are as

follows.



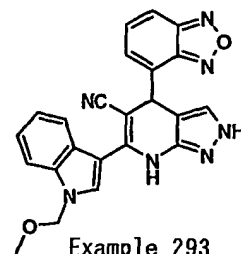
Example 290



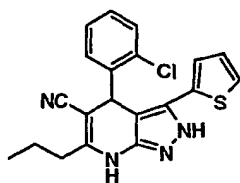
Example 291



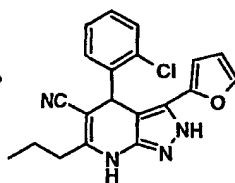
Example 292



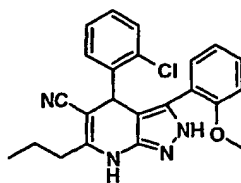
Example 293



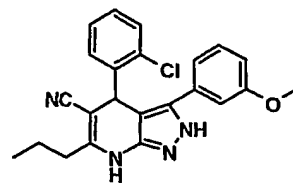
Example 294



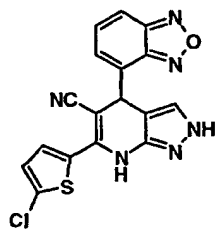
Example 295



Example 296



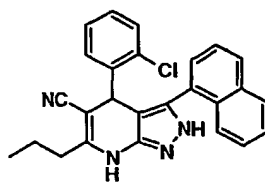
Example 297



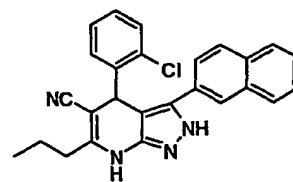
Example 298



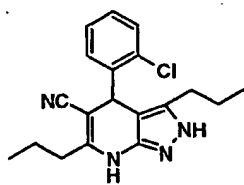
Example 299



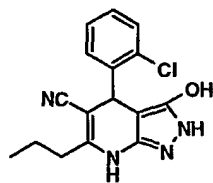
Example 300



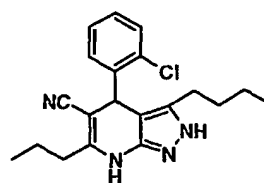
Example 301



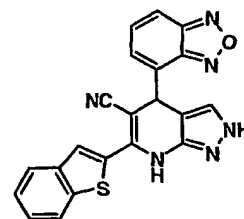
Example 302



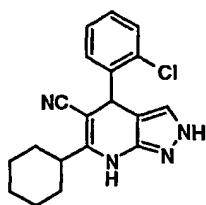
Example 303



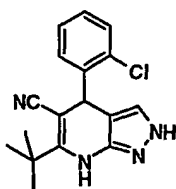
Example 304



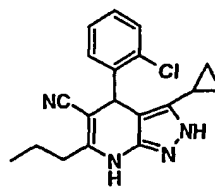
Example 305



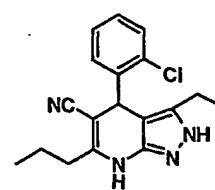
Example 306



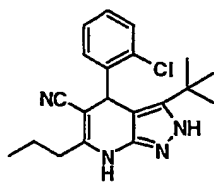
Example 307



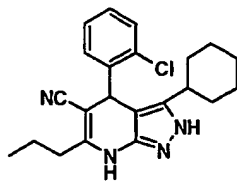
Example 308



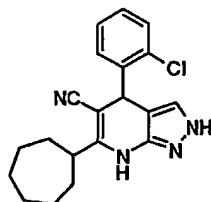
Example 309



Example 310



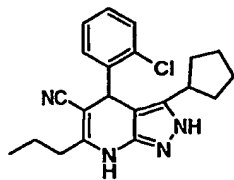
Example 311



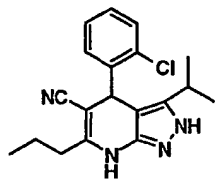
Example 312



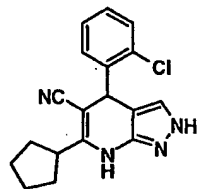
Example 313



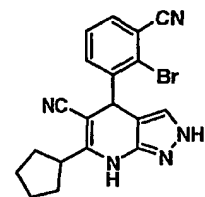
Example 314



Example 315



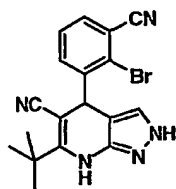
Example 316



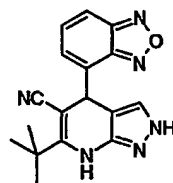
Example 317



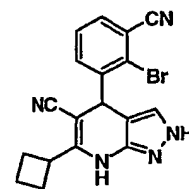
Example 318



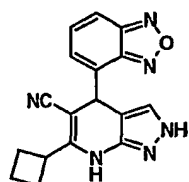
Example 319



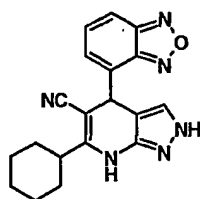
Example 320



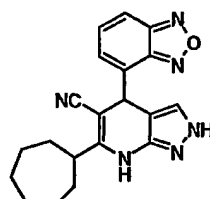
Example 321



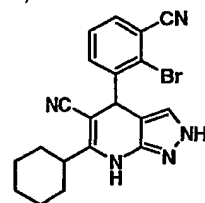
Example 322



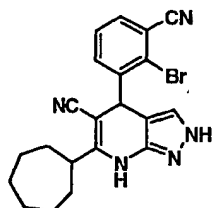
Example 323



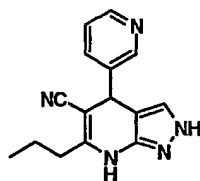
Example 324



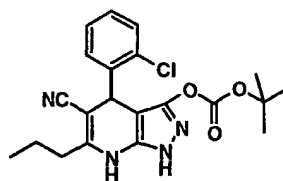
Example 325



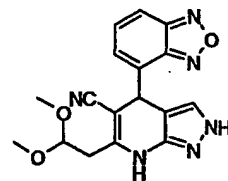
Example 326



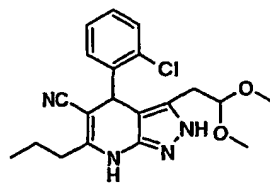
Example 327



Example 328



Example 329



Example 330



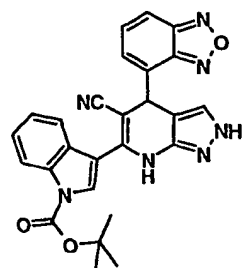
Example 331



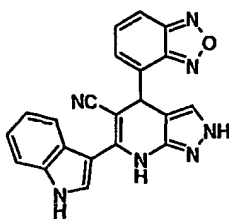
Example 332



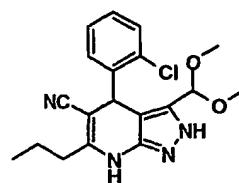
Example 333



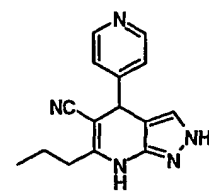
Example 334



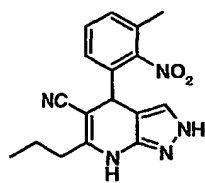
Example 335



Example 336



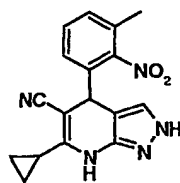
Example 337



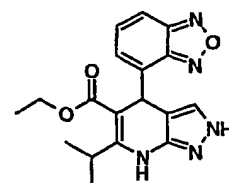
Example 338



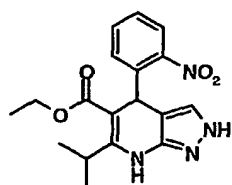
Example 339



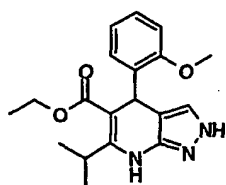
Example 340



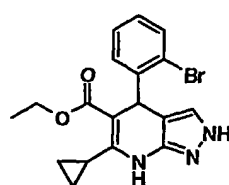
Example 341



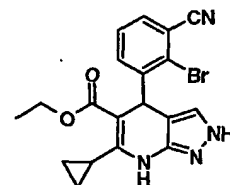
Example 342



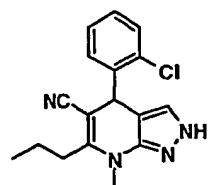
Example 343



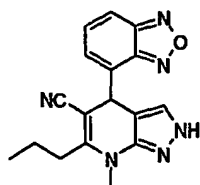
Example 344



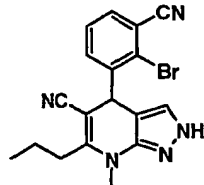
Example 345



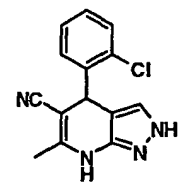
Example 346



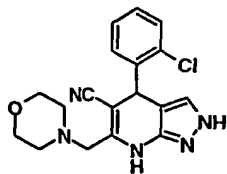
Example 347



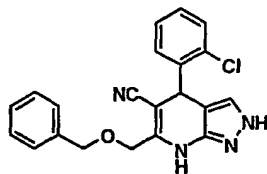
Example 348



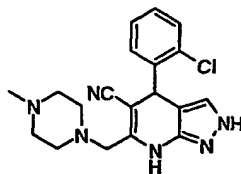
Example 349



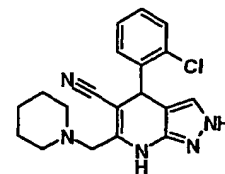
Example 350



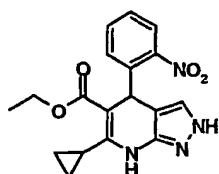
Example 351



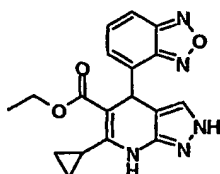
Example 352



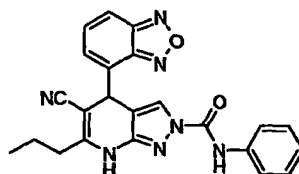
Example 353



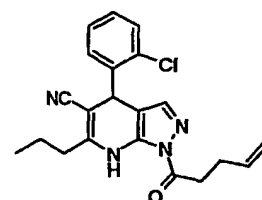
Example 354



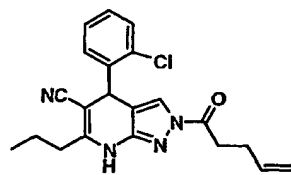
Example 355



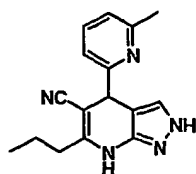
Example 356



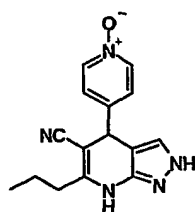
Example 357



Example 358



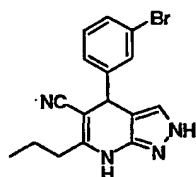
Example 359



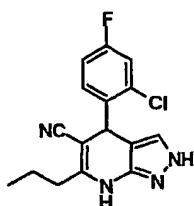
Example 360



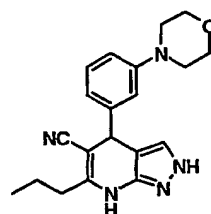
Example 361



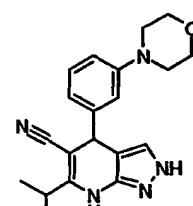
Example 362



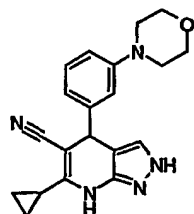
Example 363



Example 364



Example 365



Example 366

Formulation Example 1

The compound of Example 1 (0.5 part), lactose (25 parts), crystalline cellulose (35 parts) and corn starch (3 parts) were thoroughly mixed and kneaded well with a binder made of
5 corn starch (2 parts). The kneaded product was passed through a 16 mesh sieve, dried in an oven at 50°C and passed through a 4 mesh sieve. The kneaded powder thus obtained, corn starch (8 parts), crystalline cellulose (11 parts) and talc (9 parts) were thoroughly mixed and compression-punched to give tablets
10 containing 0.5 mg of the active ingredient per tablet.

Formulation Example 2

The compound of Example 1 (1.0 mg) and sodium chloride (9.0 mg) were dissolved in water for injection and the solution was filtered to remove pyrogen. The filtrate was
15 transferred into ampoules under sterile conditions. After sterilization, the ampoules were weld-sealed to give injections each containing 1.0 mg of the active ingredient.

The effects of the compounds of the present invention on glycogen synthase kinase-3 beta (GSK-3 β) were evaluated and
20 confirmed as follows.

Experimental Example 1: GSK-3 β -inhibitory activity

CREB phosphopeptide (4.6 nmol), rabbit GSK-3 β (0.5 unit), ATP (5 nmol), [γ -³²P]ATP (12.3 kBq) and a test compound were reacted in a GSK-3 β buffer solution (25 μ L) (20 mmol/L Tris-HCl
25 (pH 7.5), 10 mmol/L magnesium chloride, 5 mmol/L dithiothreitol) containing 1% dimethyl sulfoxide, at 30°C for 20 minutes. The reaction product (10 μ L) was adsorbed on a P81 ion-exchange paper, and the paper was washed with phosphoric acid (100 mmol/L) and measured for cpm on a scintillation
30 counter. As a result, the compounds of the present invention showed the IC₅₀ values of 1 to 1000 nmol/L. For example, the IC₅₀ values of the compounds of Examples 1, 14, 27, 66 and 140 were 210, 170, 25, 51 and 24 nmol/L, respectively.

CREB Phosphopeptide is Lys-Arg-Arg-Glu-Ile-Leu-Ser-Arg-Arg-Pro-Ser(P)-Tyr-Arg.

Experimental Example 2: GSK-3 β -inhibitory activity in rat cultured hippocampal neurons

5 Hippocampal neurons were obtained from rat embryos on the 18th day after conception. After culturing the hippocampal neurons for 7 days, the neurons were treated with amyloid β (25-35) (20 μ mol/L) and a test compound (GSK-3 β inhibitor) and the culture was continued for 3 hours, whereby phosphorylation
10 of Tau protein was induced. After the completion of culture, the level of phosphorylation of Tau protein was determined by EIA method using phosphorylated Tau-recognizing antibody (phosphorylated site by GSK-3 β) and the inhibitory effect of the GSK-3 β inhibitor on the neurons was evaluated. Fig. 1
15 shows the GSK-3 β -inhibitory activity of the compounds of Example 47 and Example 137.

Experimental Example 3: Effect on amyloid β -induced cytotoxicity in rat cultured hippocampal neurons

Hippocampal neurons were obtained from rat embryos on
20 the 18th day after conception. After culturing the hippocampal neurons for 7 days, the neurons were treated with amyloid β (25-35) (20 μ mol/L) and a test compound (GSK-3 β inhibitor) and the culture was continued for 24 hours, whereby cytotoxicity (decreased activity of intracellular dehydrogenases) was
25 induced. After the completion of culture, activity of intracellular dehydrogenases was determined and the effect of the GSK-3 β inhibitor on the amyloid β -induced cytotoxicity was evaluated. Fig. 2 shows the effect of the compounds of Example 66 on amyloid β -induced cytotoxicity.

30 **Experimental Example 4: GSK-3 β -inhibitory effect in gerbil brain ischemia model**

A test compound (GSK-3 β inhibitor) was intraperitoneally administered to gerbils and 30 minutes later, brain ischemia

was created by shutting off (for 4 minutes) all carotid arteries, whereby phosphorylation of Tau protein in the brain was induced. Three hours after the brain ischemia, the hippocampus was obtained from the gerbil brain and the level
5 of phosphorylation of Tau protein was determined by Western blot using phosphorylated Tau-recognizing antibody (phosphorylated site by GSK-3 β), based on which the GSK-3 β -inhibitory effect of the GSK-3 β inhibitor in the gerbil brain was evaluated. Fig. 3 shows the GSK-3 β -inhibitory effect of
10 the compounds of Example 27 in gerbil brain ischemia model.

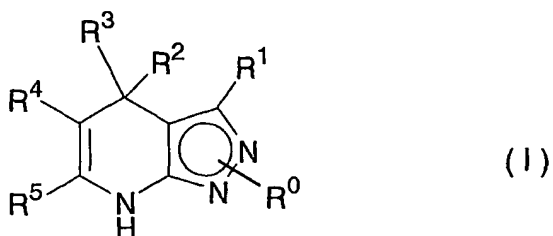
Industrial Applicability

The compounds of the present invention show a selective and strong inhibitory action on glycogen synthase kinase-3
15 beta (GSK-3 β), and are useful as medicaments for prevention and/or treatment of diabetes, diabetic complications and neurodegenerative diseases (Alzheimer's disease, ischemic cerebrovascular disorder, Down's syndrome, cerebral ischemia due to cerebral amyloid angiopathy, progressive supranuclear
20 paralysis, subacute sclerosing panencephalitic Parkinsonism, postencephalitic Parkinsonism, boxer's encephalopathy, Parkinson dementia complex of Guam, Lewy body disease, Pick's disease, corticobasal degeneration, frontotemporal dementia, AIDS encephalopathy, Huntington's disease, manic-depressive
25 psychosis and the like), or as immunopotentiators.

This application is based on patent application Nos. 2001-304707, 2001-26379 and 2001-081238 filed in Japan, the contents of which are hereby incorporated by reference.

CLAIMS

1. A dihydropyrazolopyridine compound of the formula (I):



5

wherein

R^0 is hydrogen, alkyl, acyl, cycloalkyl, formyl, haloalkyl, aminoalkyl, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, aminocarbonyl, alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, acyloxyacetyl, acyloxyalkyl, phenyl optionally having substituent(s), aromatic heterocyclic group optionally having substituent(s), phenylalkyl optionally having substituent(s), or a group of the formula: $-COOR^8$ (wherein R^8 is hydrogen, alkyl, aryl optionally having substituent(s) or aralkyl optionally having substituent(s));

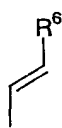
R^1 and R^2 are the same or different and each is hydrogen, alkyl, acyl, cycloalkyl, hydroxy, thiol, halogen, amino, formyl, carboxy, cyano, nitro, alkylthio, haloalkyl, aminoalkyl, acylamino, alkoxy, cycloalkoxy, phenoxy, phenylalkoxy, aminoalkoxy, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl, phenylthio, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, phenyl optionally having substituent(s), aromatic heterocyclic group or phenylalkyl;

25

20

R³ is

- (1) alkyl or haloalkyl,
- (2) cycloalkyl,
- (3) phenyl optionally having substituent(s),
- 5 (4) aromatic heterocyclic group,
- (5) a group derived from a benzene ring fused with a saturated or unsaturated 5 or 6 membered carbocyclic ring,
- (6) a group derived from a benzene ring fused with a
- 10 saturated or unsaturated 5 to 7 membered carbocyclic ring containing 1 to 3 heteroatom(s), or
- (7) a group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3 heteroatom(s), which is fused with a benzene ring,
- 15 wherein the groups of (2) to (7) may have one or more substituent(s), or
- a group selected from the groups represented by the following formulas (II) and (III),



(II)



(III)

wherein R⁶ and R⁷ are each phenyl optionally having substituent(s) or an aromatic heterocyclic group,
 or R² and R³ in conjunction form a ring optionally containing
 25 heteroatom(s), wherein the ring may be fused with a benzene ring optionally having substituent(s);
 R⁴ is alkoxycarbonyl, aminocarbonyl, hydrazinocarbonyl, alkylthiocarbonyl, formyl, carbamoyl, alkylthio, phenylthio, alkylsulfinyl, phenylsulfinyl,

alkylsulfonyl, phenylsulfonyl, dialkylphosphinyl,
dialkylphosphonyl, cyano or nitro; and
R⁵ is hydrogen, cyano, formyl, alkyl, cycloalkyl,
alkoxyalkyl, phenoxyalkyl, dialkoxyalkyl,
5 hydroxyalkyl, haloalkyl, carboxyalkyl,
cycloalkoxyalkyl, phenylthio, alkylsulfinyl,
alkylsulfonyl, phenylsulfonyl, mercaptoalkyl,
alkylthioalkyl, alkoxycarbonylalkyl,
alkoxycarbonylethenyl, aryl optionally having
10 substituent(s), an aromatic heterocyclic group or
phenylalkyl, or a group derived from a 5 to 7
membered saturated or unsaturated carbocyclic ring
containing 1 to 3 heteroatom(s), which is fused with
a benzene ring,
15 or R⁴ and R⁵ in conjunction may form a 5 or 6 membered ring
optionally containing heteroatom(s),
provided that when R⁰, R¹ and R² are each hydrogen, R⁴ is
methoxycarbonyl and R⁵ is methyl, then R³ should not
be phenyl, 2-chlorophenyl, 3-nitrophenyl, 4-
20 carboxyphenyl or 4-methoxycarbonylphenyl,
or an optically active form thereof, a pharmaceutically
acceptable salt thereof or a hydrate thereof.

2. The dihydropyrazolopyridine compound of claim 1, wherein R⁵
25 is alkyl having 2 to 8 carbon atoms, cycloalkyl, alkoxyalkyl,
phenoxyalkyl, hydroxyalkyl, phenyl optionally having
substituent(s), an aromatic heterocyclic group or phenylalkyl,
or an optically active form thereof, a pharmaceutically
acceptable salt thereof or a hydrate thereof.

30
3. The dihydropyrazolopyridine compound of claim 1, wherein R¹
is hydrogen, alkyl, phenyl optionally having substituent(s),
an aromatic heterocyclic group or phenylalkyl, or an optically

active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

4. The dihydropyrazolopyridine compound of claim 1, wherein R²
5 is hydrogen or alkyl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

5. The dihydropyrazolopyridine compound of claim 1, wherein R³
is phenyl optionally having 1 to 3 substituent(s), naphthyl,
10 2,1,3-benzoxadiazol-4-yl or 3,4-dihydro-2H-benzopyran-8-yl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

6. The dihydropyrazolopyridine compound of claim 1, wherein R⁴
15 is alkoxycarbonyl having 2 to 5 carbon atoms, cyano or nitro, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

7. The dihydropyrazolopyridine compound of claim 1, wherein R⁵
20 is alkyl having 2 to 4 carbon atoms, cyclopropyl, phenyl, thienyl or hydroxyalkyl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

8. The dihydropyrazolopyridine compound of claim 1, wherein R²
and R³ in conjunction form a ring containing sulfur atom and the ring is condensed with a benzene ring optionally having substituent(s), or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

30

9. The dihydropyrazolopyridine compound of claim 1, wherein R⁰ is hydrogen or a group of the formula: -COOR⁸ (wherein R⁸ is alkyl, aryl optionally having substituent(s) or aralkyl

optionally having substituent(s)), or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

- 5 10. The dihydropyrazolopyridine compound of claim 1, which is selected from the group consisting of
- (32) ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (47) ethyl 4-(2-chloro-3-trifluoromethylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- 10 (66) ethyl 4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (73) ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- 15 (87) ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (116) ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (122) 4-(2,3-dichlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
- 20 (140) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
- (147) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine,
- 25 (158) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine,
- (171) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine,
- (182) ethyl 4-(2-bromo-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- 30 (183) ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (189) 4-(2-bromo-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-

- 2H-pyrazolo[3,4-b]pyridine,
(205) ethyl 2-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(240) ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-ethyl-4,7-dihydro-
5 2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(257) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-pyrazolo[3,4-b]pyridine,
(260) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine,
10 (264) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine, and
(268) 4-(2-bromo-3-cyanophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine,
a tautomer, an optically active form thereof, a
15 pharmaceutically acceptable salt thereof or a hydrate thereof.

11. A medicament comprising a dihydropyrazolopyridine compound of claim 1, an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

20

12. A pharmaceutical composition comprising a dihydropyrazolopyridine compound of claim 1, an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof, and a pharmaceutically
25 acceptable additive.

13. A glycogen synthase kinase-3 beta inhibitor comprising a compound selected from the group consisting of a dihydropyrazolopyridine compound of claim 1, an optically
30 active form thereof, a pharmaceutically acceptable salt thereof and a hydrate thereof.

14. The medicament of claim 11, which is used for prevention

and/or treatment of a disease caused by glycogen synthase kinase-3 beta hyperactivity.

15. The medicament of claim 11, which is used for prevention
5 and/or treatment of a neurodegenerative disease.

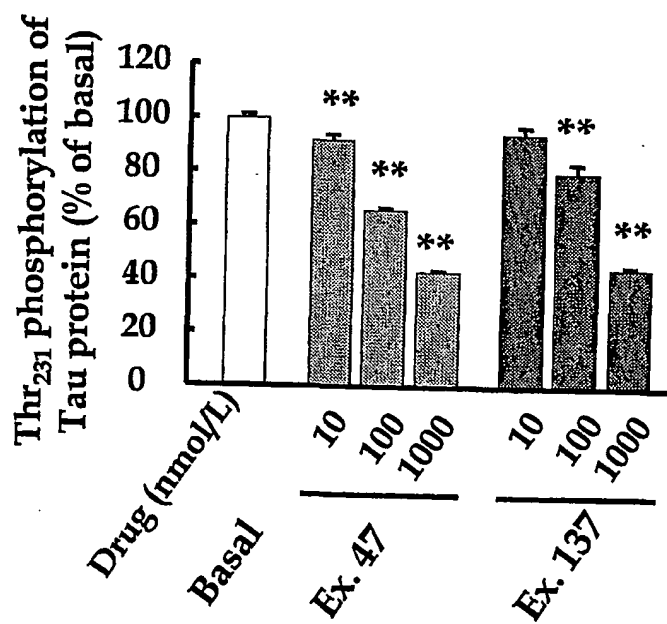
16. The medicament of claim 15, wherein the disease is
selected from the group consisting of Alzheimer's disease,
ischemic cerebrovascular disorder, Down's syndrome, cerebral
10 ischemia due to cerebral amyloid angiopathy, progressive
supranuclear paralysis, subacute sclerosing panencephalitic
Parkinsonism, postencephalitic Parkinsonism, boxer's
encephalopathy, Parkinson dementia complex of Guam, Lewy body
disease, Pick's disease, corticobasal degeneration,
15 frontotemporal dementia, AIDS encephalopathy, Huntington's
disease and manic-depressive psychosis.

17. The medicament of claim 11, which is used for prevention
and/or treatment of diabetes and diabetic complications.

20

18. The medicament of claim 11, which is used as an
immunopotentiator.

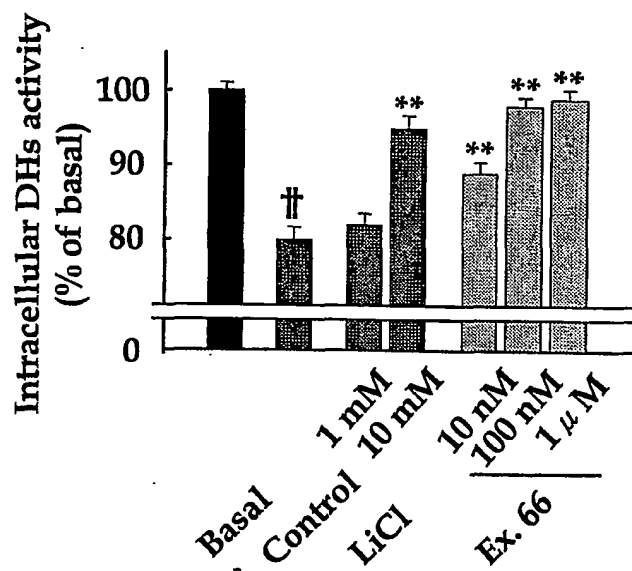
FIG. 1



Mean \pm S.E.,

** : $p < 0.01$ vs Basal by Dunnett method (n=6)

FIG. 2

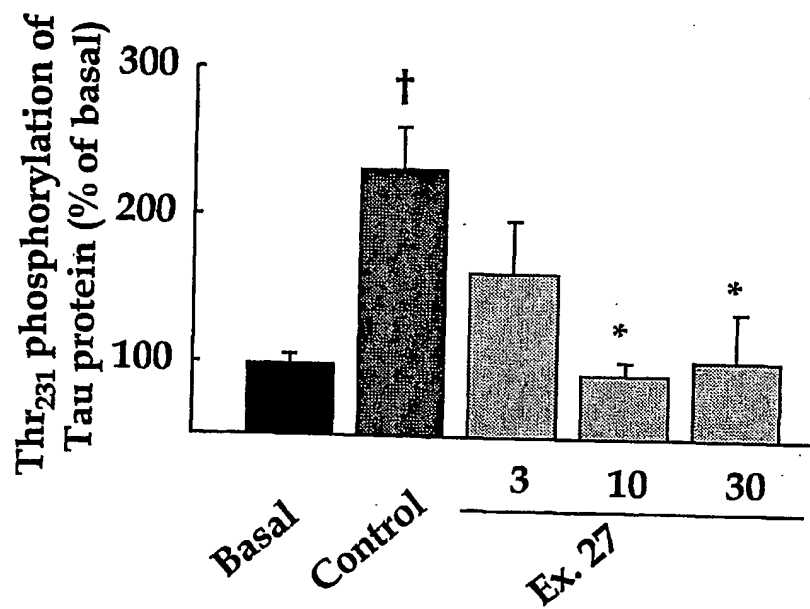


Mean \pm S.E.,

† : $p < 0.01$ vs Basal by t-test,

*: $p < 0.05$, ** : $p < 0.01$ vs Control by Dunnett method ($n=6$)

FIG. 3



Mean \pm S.E.,

†: $p < 0.05$ vs Basal by t-test,

*: $p < 0.05$ vs Control by Dunnett method ($n = 3 \sim 5$)

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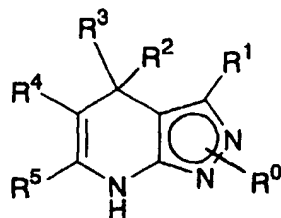
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ning of each regular issue of the PCT Gazette.*

(54) Title: DIHYDROPYRAZOLOPYRIDINE COMPOUNDS AND PHARMACEUTICAL USE THEREOF



(I)

(57) Abstract: The present invention provides dihydropy-
razolopyridine compounds represented by the formula (I):
wherein each symbol is as defined in the specification, optically
active forms thereof, and pharmaceutically acceptable salts
thereof and hydrates thereof. The compounds of the present
invention show a selective and strong inhibitory activity on
glycogen synthase kinase-3 beta (GSK-3β), and are useful
as medicaments for prevention and/or treatment of diabetes,
diabetic complications and neurodegenerative diseases or as
immunopotentiators.

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A. CLASSIFICATION OF SUBJECT MATTER
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Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 790 576 A (DE WALD H) 5 February 1974 (1974-02-05) column 7, line 50 -column 8, line 75; examples 1,2	1,2,11, 12,15,16
X	WO 92 03137 A (CHILDRENS MEDICAL CENTER) 5 March 1992 (1992-03-05) claims 1,4,5	1,2,11, 12,15,16
X	EP 0 107 619 A (SHIONOGI & CO) 2 May 1984 (1984-05-02) page 1, paragraph 2 -page 2, line 5; claim 1; examples 1-41	1,11,12, 16
X	EP 0 157 260 A (SHIONOGI & CO) 9 October 1985 (1985-10-09) page 1, paragraph 1; claim 1; example 16	1,11,12, 16
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☒ Further documents are listed in the continuation of box C.

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 146 326 A (SHIONOGI & CO) 17 April 1985 (1985-04-17) examples 8,9,13 ----	1, 11, 12, 16
X	EP 0 327 500 A (SANDOZ) 9 August 1989 (1989-08-09) example 1, step 3; example 2, step 3 ----	1, 2, 7
X	DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; QUIROGA, JAIRO ET AL: "Synthesis of 5-cyano-4,7-dihydropyrazolo'3,4-b!pyridin- 4-ones and 5-cyanopyrazolo'3,4-b!pyridin-4-ones in one-step by the reaction of 5-aminopyrazolone with benzaldehyde and benzoylacetonitrile in ethanol and by microwave radiation in dry media" retrieved from STN Database accession no. 133:321830 XP002210013 RNs 303049-48-1, 303049-49-2, 303049-50-5, 303049-51-6, 303049-52-7, 303049-53-8 & HETEROCYCLIC COMMUNICATIONS (2000), 6(3), 275-282, ----	1, 2, 7
X	EP 0 114 273 A (LEPETIT SPA) 1 August 1984 (1984-08-01) claims 1,10; examples 1-56 ----	1, 11, 12
X	IKUO ADACHI ET AL.: "Studies on dihydropyridines. Synthesis of 4,7-dihydropyrazolo'3,4-b!pyridines with vasodilating and antihypertensive activities" CHEMICAL AND PHARMACEUTICAL BULLETIN., vol. 35, no. 8, 1987, pages 3235-3252, XP002223826 PHARMACEUTICAL SOCIETY OF JAPAN. TOKYO., JP ISSN: 0009-2363 compounds 72-79, 81-98, 102, 103, 107-111, 113, 114, 144, 145, 147-150 abstract ----	1, 11, 12
X	EP 0 355 234 A (MERRELL DOW PHARMA) 28 February 1990 (1990-02-28) page 5, line 10 - line 40; example 1 ----- -/--	1, 11, 12

INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; TROSCHUETZ, REINHARD: "Synthesis of pyrido'2,3-d!pyrimidines with a trimethoprim partial structure" retrieved from STN Database accession no. 111:115132 XP002210014 RN 12232-30-5 & ARCH. PHARM. (WEINHEIM, GER.) (1989), 322(5), 285-90,</p>	1,2,7
X	<p>DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ATTABY, F.: "Reactions with cyanothioacetamide derivatives: synthesis of several new pyridine and annulated pyridine derivatives" retrieved from STN Database accession no. 114:228684 XP002223827 RN = 133707-47-8 abstract & ARCHIVES OF PHARMACAL RESEARCH (1990), 13(4), 342-6,</p>	1
X	<p>DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; DYACHENKO ET AL.: "Synthesis and properties of N- methyilmorpholinium-6-amino-3,5-dicyano-1,4 -dihydropyridine-4-spirocyclopentane-2-thi olate" retrieved from STN Database accession no. 128:140675 XP002223828 RN = '202350-12-7! & RUSSIAN CHEMICAL BULLETIN (1997), 46 (10), 1755-1757,</p>	1
A	<p>WO 99 65897 A (CHIRON CORP) 23 December 1999 (1999-12-23) abstract</p>	1,13-18

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	QUIROGA, JAIRO ET AL: "Synthesis and structural analysis of 5-cyanodihydropyrazolo'3,4- b!pyridines" JOURNAL OF HETEROCYCLIC CHEMISTRY (2001), 38(1), 53-60, XP002210012 table 1, compounds 3/4a-k ----	1,2,7
P,X	WO 01 66544 A (ABBOTT LAB) 13 September 2001 (2001-09-13) examples 1-5,7-44,48 and 32A claims 1,49 ----	1,11,12, 15
P,X	QUIROGA J ET AL: "Regioselective synthesis of 4,7,8,9-tetrahydro-2H-pyrazolo'3,4-b!quin olin-5(6H)-ones. Mechanism and structural analysis" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 57, no. 32, 6 August 2001 (2001-08-06), pages 6947-6953, XP004275098 ISSN: 0040-4020 compounds of formula 4 ----	1
P,A	WO 01 81345 A (WELFIDE) 1 November 2001 (2001-11-01) abstract -----	1,2,13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP 02/00829

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1 (in part), 2, 3-6 (in part), 7, 8 (in part), 9 (in part), 10, 11-18 (in part)

Compounds of formula I, where R5 is C2-C8 alkyl, cycloalkyl, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, phenyl optionally substituted, an aromatic heterocyclic group or phenylalkyl, and pharmaceutical compositions containing them.

2. Claims: 1, 3-6, 8, 9, 11-18 (all of them in part)

Compounds of formula I, where R5 is hydrogen, cyano, formyl, methyl, alkyl of more than 8C atoms, dialkoxyalkyl, haloalkyl, carboxyalkyl, cycloalkoxyalkyl, phenylthio, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, alkoxycarbonylalkyl, alkoxycarbonylethenyl, optionally substituted aryl but excluding phenyl, or a group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3 heteroatom(s), which is fused with a benzene ring and pharmaceutical compositions containing them.

3. Claims: 1, 11-18 (all of them in part)

Compounds of formula I where R4 and R5 together form a 5 or 6 membered ring optionally containing heteroatom(s) and pharmaceutical compositions containing them.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 02/00829

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 3790576	A	05-02-1974	NONE	
WO 9203137	A	05-03-1992	EP 0557290 A1 JP 6500554 T US 5506231 A WO 9203137 A1	01-09-1993 20-01-1994 09-04-1996 05-03-1992
EP 0107619	A	02-05-1984	JP 1639855 C JP 3006151 B JP 59065089 A AU 568092 B2 AU 1990283 A DE 3372770 D1 DK 457583 A ,B, EP 0107619 A1 ES 8502993 A1 GB 2128186 A ,B KR 9006448 B1 US 4873334 A	18-02-1992 29-01-1991 13-04-1984 17-12-1987 12-04-1984 03-09-1987 06-04-1984 02-05-1984 01-05-1985 26-04-1984 31-08-1990 10-10-1989
EP 0157260	A	09-10-1985	JP 1751089 C JP 4037834 B JP 60197685 A AU 575134 B2 AU 4007085 A DE 3578177 D1 DK 122385 A EP 0157260 A1 ES 8602787 A1 GB 2156348 A ,B KR 9106646 B1 US 4873334 A	08-04-1993 22-06-1992 07-10-1985 21-07-1988 26-09-1985 19-07-1990 20-09-1985 09-10-1985 16-03-1986 09-10-1985 30-08-1991 10-10-1989
GB 2146326	A	17-04-1985	JP 1751068 C JP 4037833 B JP 60056979 A CH 661272 A5 DE 3432985 A1 FR 2551756 A1 KR 9102838 B1 US 4562256 A	08-04-1993 22-06-1992 02-04-1985 15-07-1987 28-03-1985 15-03-1985 06-05-1991 31-12-1985
EP 0327500	A	09-08-1989	US 4822799 A EP 0327500 A2 JP 1272584 A	18-04-1989 09-08-1989 31-10-1989
EP 0114273	A	01-08-1984	AT 69227 T AU 612356 B2 AU 1470088 A AU 574654 B2 AU 2227083 A DE 3382452 D1 DK 582083 A EP 0114273 A1 ES 8601987 A1 ES 8506016 A1 FI 834661 A ,B, GR 79111 A1	15-11-1991 11-07-1991 14-07-1988 14-07-1988 28-06-1984 12-12-1991 21-06-1984 01-08-1984 01-03-1986 16-10-1985 21-06-1984 02-10-1984

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/JP 02/00829

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0114273	A		IE 57305 B1	15-07-1992
			IL 70445 A	30-12-1988
			JP 6060181 B	10-08-1994
			JP 59118786 A	09-07-1984
			KR 8902227 B1	24-06-1989
			NO 834695 A ,B,	21-06-1984
			NZ 206626 A	12-11-1986
			PH 20896 A	27-05-1987
			PT 77850 A ,B	01-01-1984
			US 4954508 A	04-09-1990
			ZA 8309092 A	25-07-1984
EP 0355234	A	28-02-1990	EP 0355234 A1	28-02-1990
			AU 619884 B2	06-02-1992
			AU 4017289 A	01-03-1990
			DK 418589 A	26-02-1990
			JP 2142728 A	31-05-1990
			ZA 8906327 A	30-05-1990
WO 9965897	A	23-12-1999	AU 4956699 A	05-01-2000
			CN 1312807 T	12-09-2001
			EP 1087963 A1	04-04-2001
			WO 9965897 A1	23-12-1999
			US 6417185 B1	09-07-2002
WO 0166544	A	13-09-2001	US 2002007059 A1	17-01-2002
			EP 1259510 A2	27-11-2002
			WO 0166544 A2	13-09-2001
WO 0181345	A	01-11-2001	AU 4878601 A	07-11-2001
			WO 0181345 A1	01-11-2001

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(21) International Application Number: PCT/JP02/00829

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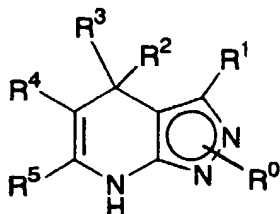
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see PCT Gazette No. 41/2002 of 10 October 2002, Section II

[Continued on next page]

WO 02/062795 A2

(54) Title: DIHYDROPYRAZOLOPYRIDINE COMPOUNDS AND PHARMACEUTICAL USE THEREOF



(I)

(57) Abstract: The present invention provides dihydropyrazolopyridine compounds represented by the formula (I): wherein each symbol is as defined in the specification, optically active forms thereof, and pharmaceutically acceptable salts thereof and hydrates thereof. The compounds of the present invention show a selective and strong inhibitory activity on glycogen synthase kinase-3 beta (GSK-3 β), and are useful as medicaments for prevention and/or treatment of diabetes, diabetic complications and neurodegenerative diseases or as immunopotentiators.



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

DESCRIPTION**DIHYDROPYRAZOLOPYRIDINE COMPOUNDS AND PHARMACEUTICAL USE
THEREOF****Technical field**

5 The present invention relates to new compounds for
medicaments, which have a glycogen synthase kinase-3 beta
(GSK-3 β)-inhibitory activity, and use thereof.

Background art

It has been reported that glycogen synthase kinase-3
10 beta (GSK-3 β), a protein kinase, is involved in the causes of
various diseases as noted in the following.

Type-II diabetes is a disease in which the insulin
reactivity of pancreatic β cells becomes low and glucose in
blood increases. As a result, complications such as diabetic
15 nephropathy, retinosis, heart disease and the like are induced.
GSK-3 β acts for inhibiting glycogen accumulation in peripheral
tissues, lowering insulin response and increasing glucose in
blood by phosphorylating glycogen synthase. Lithium having a
GSK-3 β -inhibitory activity actually lowers glucose in blood by
20 a GSK-3 β -inhibitory activity (Proc. Nat. Acad. Sci, 93, 8455
(1996)). Therefore, medicaments having a GSK-3 β -inhibitory
activity are considered to be a pharmaceutical agent effective
for the improvement of Type II diabetes and complications
thereof.

25 The developmental mechanism of Alzheimer's dementia has
not yet been elucidated. However, it is considered that
amyloid aggregation and neurofibril changes are closely
related to the cause of the development. GSK-3 β is involved in
both the amyloid aggregation and the neurofibril changes as
30 follows. (1) It binds with variant presenilin and increase
production of insoluble amyloid (Proc. Nat. Acad. Sci., 95,
9637 (1998)). (2) It causes phosphorylation of the Tau protein,
which causes neurofibril changes, and weakens the backbones of

neurons to induce neuronal death (Neurosci. Lett., 128, 195 (1991)). In addition to the above, (3) the direct involvement of GSK-3 β in neuronal death through inactivation of pyruvate dehydrogenase by phosphorylation to decrease the production
5 amount of acetylcholine necessary for maintaining cell activity (Proc. Nat. Acad. Sci., 93, 2719 (1996)) has been reported.

In addition, the effectiveness for AIDS encephalopathia as a neurodegenerative disease other than Alzheimer has been
10 suggested. Tat, which is a protein produced by HIV virus that causes AIDS, enhances GSK-3 β activity in neurons to induce neuronal death (J. Neurochem., 73, 578 (1999)). From the above, GSK-3 β inhibitors are considered to be medicaments effective for improving neurodegenerative diseases including Alzheimer's
15 dementia.

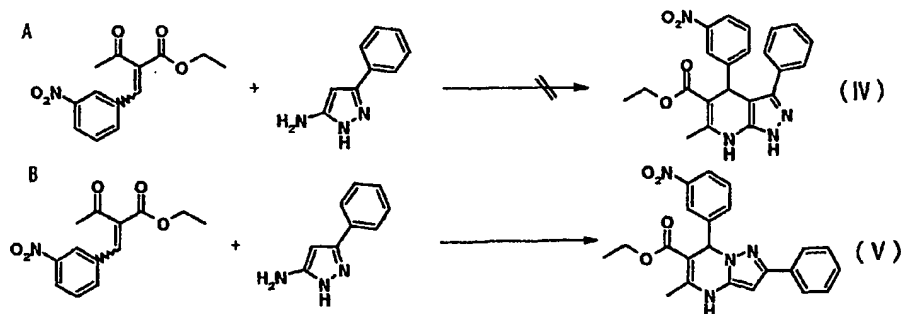
Lithium and valproic acid, which have anti-manic-depressive activity, have a GSK-3 β inhibitory activity (J. Neurochem., 72, 1327 (1999)). The relationship between anti-manic-depressive activity and GSK-3 β inhibitory activity is
20 unclear, but a suppressive activity on glutamic acid toxicity is considered to be partly responsible for maintaining neuronal activity (Proc. Nat. Acad. Sci., 95, 2642 (1998)). Based on the foregoing, GSK-3 β inhibitors are considered to be medicaments effective for improving manic-depressive psychosis.

25 NF-AT, a transcription factor, is dephosphorylated by calcineurin to increase immunological responses (Science, 275, 1930 (1997)). GSK-3 β acts for suppressing immunological function by conversely phosphorylating NF-AT. Therefore, GSK-3 β inhibitors are considered to be medicaments effective for
30 immunopotentialiation.

Incidentally, JP-A-3-272189 (invention drawn to an improved synthesis method of mevalolacton intermediates), JP-A-2-275878 (therapeutic agents for hyperlipoproteinemia and

atherosclerosis) and JP-A-1-272584 (therapeutic agents for hyperlipoproteinemia) disclose pyrazolo[3,4-b]pyridine compounds wherein the 6-position is either methyl, isopropyl or cyclopropyl. These publications do not disclose or suggest
5 any action of these compounds on GSK-3 β or the central nervous system.

The specifications of JP-A-59-65089, JP-A-59-118786, JP-A-60-56979, JP-A-60-197685 and the like disclose 6-methyl-4-substituted phenyl-4,7-dihydropyrazolo[3,4-b]pyridine-5-
10 carboxylate compounds used for the treatment of cardiovascular diseases, and they are produced by similar methods. The present inventors reproduced the following reaction A according to the method described in JP-A-59-65089, but failed
15 following) described therein. They confirmed that only the pyrazolo[1,5-a]pyrimidine derivative represented by the formula (V) could be produced. They measured IR, NMR and the melting point of the compound of the formula (V) and found them to be identical with IR, NMR and the melting point
20 described in the specification of this publication. It is therefore concluded that an erroneous structural formula has been disclosed in these publications. In other words, 6-methyl-4-substituted phenyl-4,7-dihydropyrazolo[3,4-b]pyridine-5-carboxylate cannot be synthesized according to
25 the methods described in these publications.



The compound of the above formula (IV) can be

synthesized according to the method described in J. Chem. Soc., Perkin Trans. 1, 947 (1996), and this publication discloses methyl 4-(2-chlorophenyl)-6-methyl-4,7-dihydro-1H-pyrazolo[3,4-b]pyridine-5-carboxylate and the like.

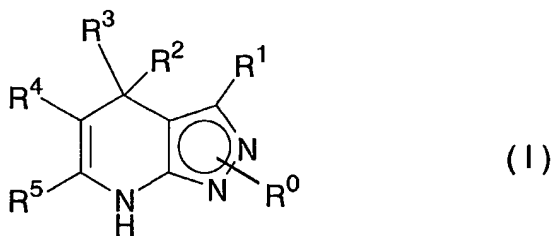
5 **Disclosure of the invention**

An object of the present invention is to provide novel compounds having a selective and strong inhibitory activity against glycogen synthase kinase-3 beta (GSK-3 β), and further, medicaments comprising them.

10 The present inventors have intensively studied to achieve the above object, and have found that 4,7-dihydropyrazolo[3,4-b]pyridine derivatives have a selective and strong inhibitory activity on GSK-3 β , which resulted in the completion of the present invention. That is, the present
15 invention relates to medicaments comprising, as an active ingredient, dihydropyrazolopyridine compounds represented by the following formula (I), which have a GSK-3 β -inhibitory activity and can be used as medicaments, optical isomers thereof, pharmaceutically acceptable salts thereof, or
20 hydrates thereof.

The present invention provides the following.

1. A dihydropyrazolopyridine compound of the formula (I):



25 wherein

R⁰ is hydrogen, alkyl, acyl, cycloalkyl, formyl, haloalkyl, aminoalkyl, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, aminocarbonyl, alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl, alkylsulfinyl,

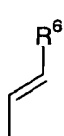
alkylsulfonyl, phenylsulfonyl, mercaptoalkyl,
alkylthioalkyl, acyloxyacetyl, acyloxyalkyl, phenyl
optionally having substituent(s), aromatic
heterocyclic group optionally having substituent(s),
5 phenylalkyl optionally having substituent(s), or a
group of the formula: $-COOR^8$ (wherein R^8 is hydrogen,
alkyl, aryl optionally having substituent(s) or
aralkyl optionally having substituent(s));

R^1 and R^2 are the same or different and each is hydrogen, alkyl,
10 acyl, cycloalkyl, hydroxy, thiol, halogen, amino,
formyl, carboxy, cyano, nitro, alkylthio, haloalkyl,
aminoalkyl, acylamino, alkoxy, cycloalkoxy, phenoxy,
phenylalkoxy, aminoalkoxy, alkoxyalkyl, phenoxyalkyl,
hydroxyalkyl, alkoxycarbonyl, aminocarbonyl,
15 alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl,
phenylthio, alkylsulfinyl, alkylsulfonyl,
phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, phenyl
optionally having substituent(s), aromatic
heterocyclic group or phenylalkyl;

20 R^3 is
(1) alkyl or haloalkyl,
(2) cycloalkyl,
(3) phenyl optionally having substituent(s),
(4) aromatic heterocyclic group,
25 (5) a group derived from a benzene ring fused with a
saturated or unsaturated 5 or 6 membered carbocyclic
ring,
(6) a group derived from a benzene ring fused with a
saturated or unsaturated 5 to 7 membered carbocyclic
30 ring containing 1 to 3 heteroatom(s), or
(7) a group derived from a 5 to 7 membered saturated
or unsaturated carbocyclic ring containing 1 to 3
heteroatom(s), which is fused with a benzene ring,

wherein the groups of (2) to (7) may have one or more substituent(s), or

a group selected from the groups represented by the following formulas (II) and (III),



(II)



(III)

wherein R^6 and R^7 are each phenyl optionally having substituent(s) or an aromatic heterocyclic group,

or R^2 and R^3 in conjunction form a ring optionally containing heteroatom(s), wherein the ring may be fused with a benzene ring optionally having substituent(s);

R^4 is alkoxycarbonyl, aminocarbonyl, hydrazinocarbonyl, alkylthiocarbonyl, formyl, carbamoyl, alkylthio, phenylthio, alkylsulfinyl, phenylsulfinyl, alkylsulfonyl, phenylsulfonyl, dialkylphosphinyl, dialkylphosphonyl, cyano or nitro; and

R^5 is hydrogen, cyano, formyl, alkyl, cycloalkyl, alkoxyalkyl, phenoxyalkyl, dialkoxyalkyl, hydroxyalkyl, haloalkyl, carboxyalkyl, cycloalkoxyalkyl, phenylthio, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, alkoxycarbonylalkyl, alkoxycarbonylethenyl, aryl optionally having substituent(s) (particularly phenyl), an aromatic heterocyclic group or phenylalkyl, or a group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3 heteroatom(s), which is fused with a benzene ring,

or R^4 and R^5 in conjunction may form a 5 or 6 membered ring optionally containing heteroatom(s),

- provided that when R^0 , R^1 and R^2 are each hydrogen, R^4 is methoxycarbonyl and R^5 is methyl, then R^3 should not be phenyl, 2-chlorophenyl, 3-nitrophenyl, 4-carboxyphenyl or 4-methoxycarbonylphenyl,
- 5 or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.
2. The dihydropyrazolopyridine compound of the above-described 1, wherein R^5 is alkyl having 2 to 8 carbon atoms, cycloalkyl, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, phenyl optionally
- 10 having substituent(s), an aromatic heterocyclic group or phenylalkyl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.
3. The dihydropyrazolopyridine compound of the above-described 1, wherein R^1 is hydrogen, alkyl, phenyl optionally having
- 15 substituent(s), an aromatic heterocyclic group or phenylalkyl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.
4. The dihydropyrazolopyridine compound of the above-described 1, wherein R^2 is hydrogen or alkyl, or an optically active form
- 20 thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.
5. The dihydropyrazolopyridine compound of the above-described 1, wherein R^3 is phenyl optionally having 1 to 3 substituent(s), naphthyl, 2,1,3-benzoxadiazol-4-yl or 3,4-dihydro-2H-
- 25 benzopyran-8-yl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.
6. The dihydropyrazolopyridine compound of the above-described 1, wherein R^4 is alkoxy carbonyl having 2 to 5 carbon atoms, cyano or nitro, or an optically active form thereof, a
- 30 pharmaceutically acceptable salt thereof or a hydrate thereof.
7. The dihydropyrazolopyridine compound of the above-described 1, wherein R^5 is alkyl having 2 to 4 carbon atoms, cyclopropyl, phenyl, thienyl or hydroxyalkyl, or an optically active form

thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

8. The dihydropyrazolopyridine compound of the above-described 1, wherein R^2 and R^3 in conjunction form a ring containing
5 sulfur atom and the ring is condensed with a benzene ring optionally having substituent(s), or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

9. The dihydropyrazolopyridine compound of the above-described
10 1, wherein R^0 is hydrogen or a group of the formula: $-\text{COOR}^8$ (wherein R^8 is alkyl, aryl optionally having substituent(s) or aralkyl optionally having substituent(s)), or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

15 10. The dihydropyrazolopyridine compound of the above-described 1, which is selected from

(32) ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,

(47) ethyl 4-(2-chloro-3-trifluoromethylphenyl)-4,7-dihydro-6-
20 propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,

(66) ethyl 4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,

(73) ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,

25 (87) ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,

(116) ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,

(122) 4-(2,3-dichlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-
30 pyrazolo[3,4-b]pyridine,

(140) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine,

(147) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-phenyl-

- 2H-pyrazolo[3,4-b]pyridine,
(158) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine,
(171) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-
5 (thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine,
(182) ethyl 4-(2-bromo-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(183) ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
10 (189) 4-(2-bromo-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
(205) ethyl 2-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(240) ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-ethyl-4,7-dihydro-
15 2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(257) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-pyrazolo[3,4-b]pyridine,
(260) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine,
20 (264) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine, and
(268) 4-(2-bromo-3-cyanophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine,
a tautomer, an optically active form thereof, a
25 pharmaceutically acceptable salt thereof or a hydrate thereof.
11. A medicament comprising a dihydropyrazolopyridine compound of the above-described 1, an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.
12. A pharmaceutical composition comprising a
30 dihydropyrazolopyridine compound of the above-described 1, an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof, and a pharmaceutically acceptable additive.

13. A glycogen synthase kinase-3 beta inhibitor comprising a compound selected from the group consisting of a dihydropyrazolopyridine compound of the above-described 1, an optically active form thereof, a pharmaceutically acceptable salt thereof and a hydrate thereof.
14. The medicament of the above-described 11, which is used for prevention and/or treatment of a disease caused by glycogen synthase kinase-3 beta hyperactivity.
15. The medicament of the above-described 11, which is used for prevention and/or treatment of a neurodegenerative disease.
16. The medicament of the above-described 15, wherein the disease is selected from the group consisting of Alzheimer's disease, ischemic cerebrovascular disorder, Down's syndrome, cerebral ischemia due to cerebral amyloid angiopathy, progressive supranuclear paralysis, subacute sclerosing panencephalitic Parkinsonism, postencephalitic Parkinsonism, boxer's encephalopathy, Parkinson dementia complex of Guam, Lewy body disease, Pick's disease, corticobasal degeneration, frontotemporal dementia, AIDS encephalopathy, Huntington's disease and manic-depressive psychosis.
17. The medicament of the above-described 11, which is used for prevention and/or treatment of diabetes and diabetic complications.
18. The medicament of the above-described 11, which is used as an immunopotentiator.

Brief Description of The Drawings

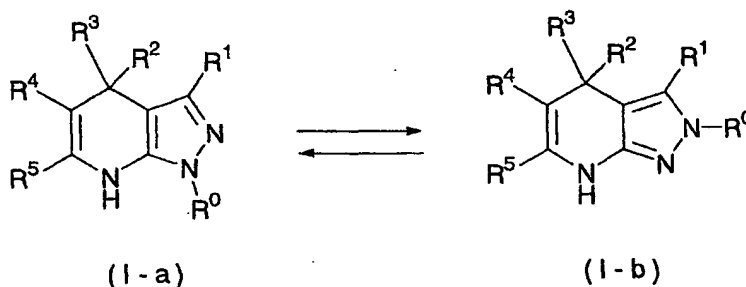
Fig. 1 shows the GSK-3 β -inhibitory activity of the compounds of Example 47 and Example 137.

Fig. 2 shows the effect of the compound of Example 66 on amyloid β -induced cytotoxicity.

Fig. 3 shows the GSK-3 β -inhibitory effect of the compound of Example 27 in a gerbil brain ischemia model.

Detailed Description of The Invention

The formula (I) indicates the presence of tautomers represented by the following formulas (I-a) and (I-b), based on the positions of hydrogen atoms of the pyrazole ring. The present invention encompasses each isomer of formulas (I-a) and (I-b), and a mixture of these isomers.



The compounds represented by the formula (I) in the present specification are described in detail in the following.

"Alkyl" means a linear or branched carbon chain of 1 to 8 carbon atom(s), and includes methyl, ethyl, propyl, butyl, pentyl(amyl), hexyl, or a structural isomer thereof, such as isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl, tert-pentyl and the like, with a preference for alkyl having 1 to 4 carbon atom(s). The alkyl of R⁵ is preferably alkyl having 2 to 8 carbon atoms. The "alkyl having 2 to 8 carbon atoms" concretely includes ethyl, propyl, butyl, pentyl(amyl), hexyl, heptyl and octyl, or a structural isomer thereof, such as isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl, tert-butyl and the like. Alkyl having 2 to 4 carbon atoms is more preferable, and propyl is particularly preferable.

"Acyl" includes alkylcarbonyl having 2 to 8 carbon atoms, such as acetyl, propionyl, butyryl, isobutyryl, valeryl, pivaloyl, hexanoyl, heptanoyl and the like, and aromatic acyl having 7 to 12 carbon atoms, such as benzoyl, naphthoyl, cinnamoyl, benzylcarbonyl and the like. The benzene and naphthalene rings may have 1 to 5 substituent(s).

"Cycloalkyl" means a cyclic carbon chain of 3 to 8 carbon atoms. Cycloalkyl concretely includes, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and the like, with a preference for cycloalkyl having 3 to 6 carbon atoms.

"Halogen" represents fluorine, chlorine, bromine or iodine.

"Amino" is primary amino, or secondary or tertiary amino having the above alkyl, and includes, for example, amino, methylamino, dimethylamino, ethylamino, diethylamino, propylamino, dipropylamino, butylamino, dibutylamino and the like, with a preference for tertiary amino containing alkyl having 1 to 4 carbon atom(s).

"Alkylthio" is a linear or branched alkylthio having 1 to 6 carbon atom(s), and includes, for example, methylthio, ethylthio, propylthio, butylthio, pentylthio(amythio), hexylthio and structural isomers thereof, such as isopropylthio, isobutylthio, sec-butylthio, tert-butylthio, isopentylthio, neopentylthio, tert-pentylthio and the like, with a preference for alkylthio having 1 to 3 carbon atom(s).

"Haloalkyl" is the above alkyl substituted by 1 to 5 halogen(s), and represents fluoromethyl, chloromethyl, difluoromethyl, trifluoromethyl, 2,2,2-trifluoroethyl, 2,2,3,3,3-pentafluoropropyl and the like.

"Aminoalkyl" is the above-mentioned alkyl having the above amino, and includes, for example, aminomethyl, methylaminomethyl, dimethylaminomethyl, 2-aminoethyl, 2-methylaminoethyl, 2-dimethylaminoethyl, 2-ethylaminoethyl, 2-diethylaminoethyl and the like, with a preference for aminoalkyl containing alkyl having 1 to 4 carbon atom(s) having tertiary amino.

"Acylamino" is acylamino having the above acyl, and represents, for example, acetylamino, propionylamino,

butyrylamino, valerylamino, pivaloylamino, benzoylamino, phenylacetylamino, phenylpropionylamino, phenylbutyrylamino and the like.

"Alkoxy" is alkoxy having the above alkyl, and includes,
5 for example, methoxy, ethoxy, propoxy, butoxy, pentyloxy(amyloxy), hexyloxy and structural isomers thereof, such as isopropoxy, isobutoxy, sec-butoxy, tert-butoxy, isopentyloxy, neopentyloxy, tert-pentyloxy and the like, with a preference for alkoxy having 1 to 4 carbon atom(s).

10 "Cycloalkoxy" is alkoxy having the above cycloalkyl, and includes, for example, cyclopropoxy, cyclobutoxy, cyclopentyloxy, cyclohexyloxy and the like, with a preference for cycloalkoxy having cycloalkyl having 3 to 6 carbon atoms.

"Phenylalkoxy" is phenylalkoxy having the above alkoxy,
15 and includes, for example, benzyloxy, 1-phenylethoxy, 2-phenylethoxy, 3-phenylpropoxy, 4-phenylbutoxy, 1-methyl-1-phenylethoxy, 1-methyl-2-phenylethoxy, 1-phenylpropoxy, 2-phenylpropoxy, 1-methyl-1-phenylpropoxy, 1-methyl-2-phenylpropoxy, 1-methyl-3-phenylpropoxy and the like, with a
20 preference for phenylalkoxy containing alkoxy having 1 to 4 carbon atom(s).

"Aminoalkoxy" is aminoalkoxy consisting of the above alkoxy and amino, and includes, for example, aminomethoxy, methylaminomethoxy, dimethylaminomethoxy, 2-
25 dimethylaminoethoxy, 3-dimethylaminopropoxy, 4-dimethylaminobutoxy and the like, with a preference for aminoalkoxy consisting of tertiary amino containing alkyl having 1 to 4 carbon atom(s), and alkoxy having 1 to 4 carbon atom(s).

30 "Alkoxyalkyl" is alkoxyalkyl consisting of the above alkoxy and alkyl, and includes, for example, methoxymethyl, ethoxymethyl, 2-methoxyethyl, propoxymethyl, isopropoxymethyl and the like, with a preference for alkoxyalkyl consisting of

alkoxy having 1 to 4 carbon atom(s) and alkyl having 1 to 4 carbon atom(s).

"Phenoxyalkyl" is phenoxyalkyl containing the above alkyl, and includes, for example, phenoxymethyl, 2-phenoxyethyl, 3-phenoxypropyl and the like, with a preference for phenoxyalkyl containing alkyl having 1 to 4 carbon atom(s).

"Dialkoxyalkyl" is dialkoxyalkyl consisting of the above alkyl and alkoxy, and includes, for example, dimethoxymethyl, diethoxymethyl, 2,2-dimethoxyethyl, 2,2-diethoxyethyl and the like, with a preference for dialkoxyalkyl consisting of alkoxy having 1 to 4 carbon atom(s) and alkyl having 1 to 4 carbon atom(s).

"Hydroxyalkyl" is hydroxyalkyl having the above alkyl, and includes, for example, hydroxymethyl, 2-hydroxyethyl, 3-hydroxypropyl and the like, with a preference for hydroxyalkyl containing alkyl having 1 to 4 carbon atom(s).

"Alkoxy carbonyl" is alkoxy carbonyl having the above alkoxy, and includes, for example, methoxy carbonyl, ethoxy carbonyl, propoxy carbonyl, butoxy carbonyl, pentyloxy carbonyl, hexyloxy carbonyl and structural isomers thereof, such as isopropoxy carbonyl, isobutoxy carbonyl, sec-butoxy carbonyl, tert-butoxy carbonyl, isopentyloxy carbonyl, neopentyloxy carbonyl, tert-pentyloxy carbonyl and the like, with a preference for alkoxy carbonyl, in which the alkoxy moiety has 1 to 4 carbon atom(s). However, R⁴ is preferably alkoxy carbonyl having 2 to 5 carbon atoms.

"Amino carbonyl" is amino carbonyl having the above amino, and includes, for example, amino carbonyl (carbamoyl), methylaminocarbonyl, dimethylaminocarbonyl, ethylaminocarbonyl, diethylaminocarbonyl, propylaminocarbonyl, dipropylaminocarbonyl, phenylcarbamoyl, benzylcarbamoyl and the like, with a preference for tertiary-amino carbonyl containing alkyl having 1 to 4 carbon atom(s).

"Alkylthiocarbonyl" is alkylthiocarbonyl having the above alkylthio, and includes, for example, methylthiocarbonyl, ethylthiocarbonyl, propylthiocarbonyl, butylthiocarbonyl and structural isomers thereof, such as isopropylthiocarbonyl, 5 isobutylthiocarbonyl, sec-butylthiocarbonyl, tert-butylthiocarbonyl and the like, with a preference for alkylthiocarbonyl, in which the alkyl moiety has 1 to 3 carbon atoms.

"Carboxyalkyl" is carboxyalkyl having the above alkyl, 10 and includes, for example, carboxymethyl, carboxyethyl, carboxypropyl and the like, with a preference for carboxyalkyl containing alkyl having 1 to 4 carbon atom(s).

"Cycloalkoxyalkyl" is cycloalkoxyalkyl having the above cycloalkoxy and alkyl, and includes, for example, 15 cyclopropoxymethyl, cyclopropoxyethyl, cyclobutoxymethyl, cyclopentyloxymethyl, cyclohexyloxymethyl and the like, with a preference for cycloalkoxyalkyl consisting of cycloalkoxy having 3 to 6 carbon atoms and alkyl having 1 to 4 carbon atom(s).

20 "Alkylsulfinyl" is alkylsulfinyl having the above alkyl, and includes, for example, methylsulfinyl, ethylsulfinyl, propylsulfinyl, isopropylsulfinyl and the like, with a preference for alkylsulfinyl containing alkyl having 1 to 4 carbon atom(s).

25 "Alkylsulfonyl" is alkylsulfonyl having the above alkyl, and includes, for example, methylsulfonyl, ethylsulfonyl, propylsulfonyl, isopropylsulfonyl and the like, with a preference for alkylsulfonyl containing alkyl having 1 to 4 carbon atom(s).

30 "Mercaptoalkyl" is mercaptoalkyl having the above alkyl, and includes, for example, mercaptomethyl, mercaptoethyl, mercaptopropyl and the like, with a preference for mercaptoalkyl containing alkyl having 1 to 4 carbon atom(s).

"Alkylthioalkyl" is alkylthioalkyl having the above alkylthio and alkyl, and includes, for example, methylthiomethyl, methylthioethyl, methylthiopropyl, ethylthiomethyl, ethylthioethyl, ethylthiopropyl and the like, with a preference for alkylthioalkyl consisting of alkylthio having 1 to 3 carbon atom(s) and alkyl having 1 to 4 carbon atom(s).

"Aryl" is aryl having 6 to 14 carbon atoms, and includes, for example, phenyl, 1-naphthyl, 2-naphthyl, 1-anthryl, 2-anthryl and the like. They may have 1 to 5 substituent(s) and substitution sites are not particularly limited.

"Aralkyl" is aralkyl wherein the above alkyl is substituted by the above aryl, and includes benzyl, 2-phenylethyl, 3-phenylpropyl, 1-naphthylmethyl, 2-naphthylmethyl and the like. These may have 1 to 5 substituent(s) on the aryl moiety.

"Acyloxyacetyl" is acyloxyacetyl having the above acyl, and includes, for example, acetyloxyacetyl, propionyloxyacetyl, butyryloxyacetyl, benzoyloxyacetyl and the like.

"Acyloxyalkyl" is acyloxyalkyl having the above acyl and alkyl, and includes, for example, acetyloxymethyl, propionyloxymethyl, butyryloxymethyl, benzoyloxymethyl, 2-acetyloxyethyl, 2-propionyloxyethyl, 2-butyryloxyethyl, 2-benzoyloxyethyl and the like.

The substituent of the "phenyl optionally having substituent(s)" is exemplified by those mentioned for the "substituent" below, wherein the number of the substituent is generally 1 to 5, preferably 3. Phenyl having 1 or 2 substituent(s) is particularly preferable.

"Aromatic heterocyclic group" is a 5- or 6-membered aromatic heterocyclic ring optionally containing 1 to 3 heteroatom(s) of nitrogen atom, oxygen atom and sulfur atom, and includes, for example, thiophene, furan, pyrrole,

imidazole, pyrazole, thiazole, isothiazole, oxazole, isoxazole, pyridine, pyridazine, pyrimidine, pyrazine and the like.

The substituent of the "aromatic heterocyclic ring optionally having substituent(s)" is exemplified by those
5 mentioned for the "substituent" below, wherein the number of the substituent is generally 1 to 5, preferably 3.

"Phenylalkyl" is phenylalkyl having the above alkyl, and includes, for example, benzyl, 2-phenylethyl, 3-phenylpropyl, 4-phenylbutyl, 1-phenylethyl, 1-methyl-2-phenylethyl, 1-
10 phenylpropyl, 2-phenylpropyl, 1-methyl-1-phenylpropyl, 1-methyl-2-phenylpropyl, 1-methyl-3-phenylpropyl and the like, with a preference for phenylalkyl consisting of phenyl and alkyl having 1 to 4 carbon atom(s).

The kind and the number of the substituent of the
15 "phenylalkyl optionally having substituent(s)" are the same as those for the above-mentioned "aromatic heterocyclic ring".

"Alkoxy carbonylalkyl" is alkoxy carbonylalkyl having the above alkoxy carbonyl and alkyl, and includes, for example, methoxycarbonylmethyl, ethoxycarbonylmethyl,
20 ethoxycarbonylmethyl, 2-ethoxycarbonylethyl, 3-ethoxycarbonylpropyl and the like.

"Alkoxy carbonylethenyl" is alkoxy carbonylethenyl having the above alkoxy carbonyl, and includes, for example, 2-methoxycarbonylethenyl, 2-ethoxycarbonylethenyl, 2-
25 butoxycarbonylethenyl, 2-tert-butoxycarbonylethenyl and the like.

"Dialkylphosphinyl" is dialkylphosphinyl having the above alkyl, and includes, for example, dimethylphosphinyl, diethylphosphinyl, dipropylphosphinyl and the like, with a
30 preference for dialkylphosphinyl containing alkyl having 1 to 4 carbon atom(s).

"Dialkylphosphonyl" is dialkylphosphonyl having the above alkyl, and includes, for example, dimethylphosphonyl,

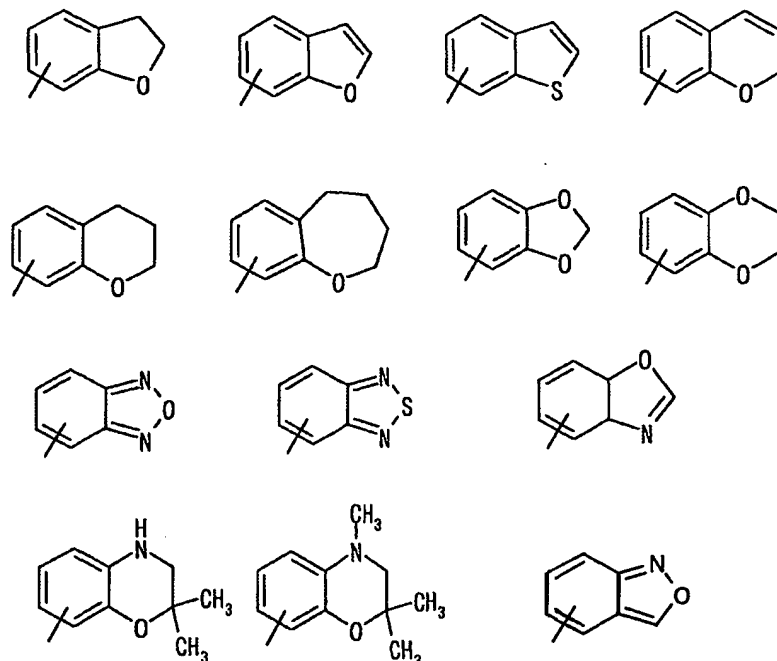
diethylphosphonyl, dipropylphosphonyl and the like, with a preference for dialkylphosphonyl containing alkyl having 1 to 4 carbon atom(s).

In the present specification, "substituent" includes
5 alkyl, acyl, cycloalkyl, phenyl, aromatic heterocyclic ring, phenylalkyl, hydroxy, thiol, halogen, amino, formyl, carbamoyl, cyano, nitro, alkylthio, haloalkyl, aminoalkyl, acylamino, alkoxy, cycloalkoxy, phenoxy, phenylalkoxy, aminoalkoxy, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, alkoxycarbonyl,
10 alkylsulfinyl, aminocarbonyl, alkylthiocarbonyl and the like.

"Ring optionally containing heteroatom(s)" is a 5 or 6 membered carbocyclic ring optionally containing 1 to 3 heteroatom(s) consisting of nitrogen atom, oxygen atom and sulfur atom, with particular preference given to a ring
15 containing sulfur atom. The ring may be substituted by one or more of the above substituents or oxo groups. The substitution site is not particularly limited. This ring is formed by R^2 and R^3 in the formula (I) together with the attached carbon atom. By forming this ring, a spiro ring is formed in the
20 compound of the formula (I). The above ring can be fused with a benzene ring optionally having substituent(s). Such a ring includes, for example, 2,3-dihydrobenzo[b]thiophene, 2,3-dihydrobenzo[b]thiophen-1-oxide and the like.

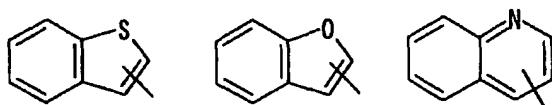
"A group derived from a benzene ring, which is fused
25 with a saturated or unsaturated 5 or 6 membered carbocyclic ring" represents a group derived from naphthalene, 1,2-dihydronaphthalene, 1,2,3,4-tetrahydronaphthalene, indan and the like, with preference given to naphthalene (namely naphthyl) and particular preference given to 1-naphthyl.

30 "A group derived from a benzene ring fused with a saturated or unsaturated 5 to 7 membered carbocyclic ring containing 1 to 3 heteroatom(s)" includes the following groups and the like.



Of these, 2,1,3-benzoxadiazole and 3,4-dihydro-2H-benzopyrane are preferable, and 2,1,3-benzoxadiazol-4-yl and 3,4-dihydro-2H-benzopyran-8-yl are particularly preferable.

5 "A group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3 heteroatom(s), which is fused with a benzene ring" includes the following groups and the like.



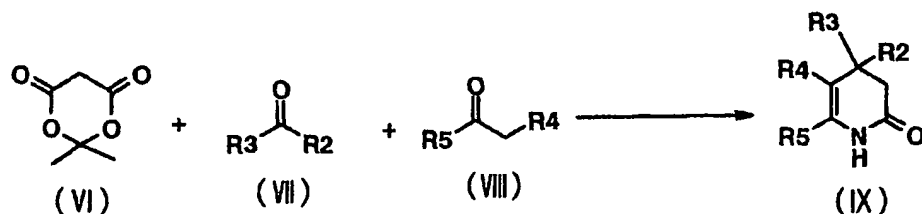
10 The "5 or 6-membered ring optionally containing heteroatom(s)" is a 5 or 6 membered carbocyclic ring optionally containing 1 to 3 heteroatom(s) consisting of nitrogen atom, oxygen atom and sulfur atom. Examples thereof include furan, thiophene, pyrrole, oxazole, isoxazole, 15 thiazole, isothiazole, imidazole, pyrazole, furazan, pyran, pyridine, pyridazine, pyrimidine, pyrazine, pyrroline, pyrrolidine, imidazoline and imidazolidine. Of these, furan,

thiophene, pyrrole, oxazole, isoxazole, thiazole, isothiazole, furazan and pyridine are preferable.

The compounds, represented by the formula (I) of the present invention can be converted to acid addition salts with
 5 pharmaceutically acceptable acids and such acid addition salts are also encompassed in the present invention. Such acid addition salts include, for example, salts with inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, nitric acid, phosphoric acid and the like,
 10 and salts with organic acids such as formic acid, acetic acid, propionic acid, oxalic acid, malonic acid, succinic acid, fumaric acid, maleic acid, lactic acid, malic acid, citric acid, tartaric acid, methanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid, glutamic acid and the like.

15 Furthermore, the compounds of the present invention can form hydrates, solvates with ethanol and the like, and crystal polymorphs. When an asymmetric carbon atom exists, optical isomers and racemates thereof can be present, and all of these are encompassed in the present invention.

20 Of the compounds (I) of the present invention, a compound wherein R⁰ is hydrogen can be synthesized as shown in the following according to the method described in J. Chem. Soc., Perkin Trans. 1, 947 (1996) and the like.
 (First Production Method)

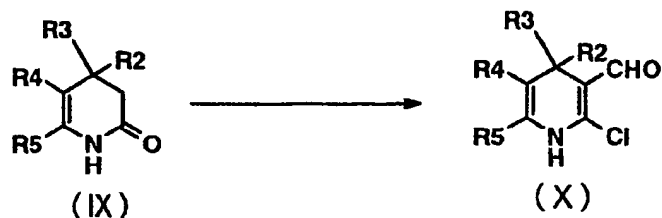


25

wherein R², R³, R⁴ and R⁵ are as defined above.

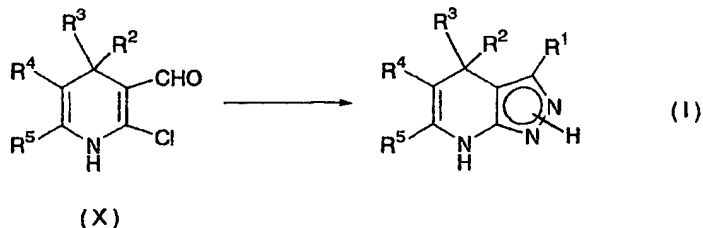
Meldrum's acid of the formula (VI) and a carbonyl derivative of the formula (VII) are reacted with a carbonyl

derivative of the formula (VIII) to give an amide derivative of the formula (IX). The reaction is carried out in the presence of a carboxylic acid solvent inert to the reaction. As the solvent, formic acid, acetic acid, propionic acid, butyric acid, valeric acid and the like are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.



wherein R², R³, R⁴ and R⁵ are as defined above.

The obtained amide derivative of the formula (IX) is reacted in the presence of dimethylformamide and phosphorus oxychloride to give a formyl derivative of the formula (X). The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, ether, tetrahydrofuran, dioxane, ethyl acetate, acetonitrile, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethyl sulfoxide and the like are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.



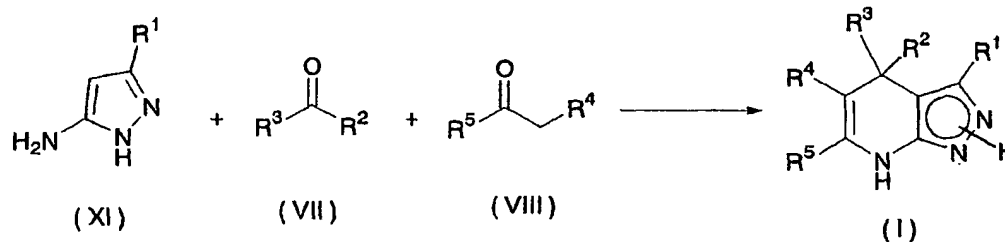
wherein R¹ represents hydrogen, and R², R³, R⁴ and R⁵ are as defined above.

The compound (I) of the present invention can be produced by reacting the obtained formyl derivative of the

formula (X) in the presence of hydrazine. The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, ether, tetrahydrofuran, dioxane, ethyl acetate, acetonitrile, benzene, toluene, chloroform, dichloromethane, 5 dimethylformamide, dimethyl sulfoxide, pyridine, alcohol and the like are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.

The carbonyl derivative of the formula (VII), which is a 10 starting material, can be synthesized according to the methods described in J. Org. Chem., 46, 783 (1981), Eur. J. Med. Chem., 31, 3 (1996) and Tetrahedron Lett., 24, 5023 (1983). The carbonyl derivative of the formula (VIII) can be synthesized according to the method described in Synthesis, 290 (1993).

15 (Second Production Method)

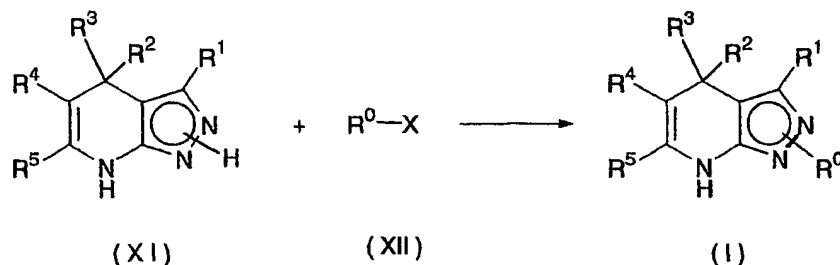


wherein R¹, R², R³, R⁴ and R⁵ are as defined above.

The compounds (I) of the present invention can be produced by reacting aminopyrazole of the formula (XI) and a 20 carbonyl derivative of the formula (VII) with a carbonyl derivative of the formula (VIII). The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, ether, tetrahydrofuran, dioxane, ethyl acetate, acetonitrile, benzene, toluene, chloroform, dichloromethane, 25 dimethylformamide, dimethyl sulfoxide, alcohol and the like are generally used. The reaction is carried out at any temperature, for example, from 0°C to 200°C, preferably from 60°C to 100°C.

Of the compounds (I) of the present invention, a compound wherein R^0 is a substituent other than hydrogen can be synthesized as follows.

(Third Production Method)

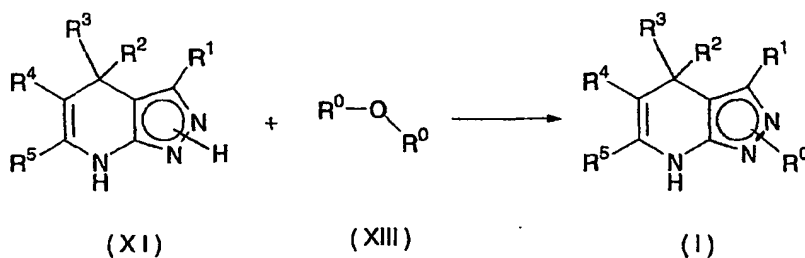


5

wherein R^0 , R^1 , R^2 , R^3 , R^4 and R^5 are as defined above, and X represents halogen, provided that R^0 is not hydrogen.

The compounds (I) of the present invention can be produced by reacting a dihydropyrazolopyridine derivative of the formula (XI) with halide of the formula (XII) in the presence of a base. Suitable base includes, for example, triethylamine, diisopropylethylamine, 4-dimethylaminopyridine and the like. The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, one without hydroxy group is generally used, such as tetrahydrofuran, ethyl acetate, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethylimidazolidinone and the like. The reaction is carried out at any temperature, for example, from -10°C to 200°C , preferably from 0°C to 100°C .

20 (Fourth Production Method)



wherein R^0 , R^1 , R^2 , R^3 , R^4 and R^5 are as defined above, provided

that R⁰ is not hydrogen.

The compounds (I) of the present invention can be produced by reacting a dihydropyrazolopyridine derivative of the formula (XI) with anhydride of the formula (XIII) in the presence of a base. Suitable base includes, for example, triethylamine, pyridine, 4-dimethylaminopyridine and the like. The reaction is carried out in the presence of a solvent inert to the reaction. As the solvent, one without hydroxy group is generally used, such as tetrahydrofuran, ethyl acetate, benzene, toluene, chloroform, dichloromethane, dimethylformamide, dimethylimidazolidinone, pyridine and the like. The reaction is carried out at any temperature, for example, from -10°C to 200°C, preferably from 0°C to 100°C.

The compound (I) of the present invention thus produced can be isolated and purified as a free compound or a salt thereof. Isolation and purification is carried out by a conventional chemical process such as extraction, concentration, evaporation, crystallization, filtration, recrystallization, various kinds of chromatography and the like. When the purified product obtained is a racemate, a desired optically active compound can be separated by, for example, fractional recrystallization with optically active acid, or passing through a column packed with optically active carrier. The present invention also encompasses optically active compounds.

The compounds of the present invention obtained by the above methods have a weak inhibitory activity on kinases other than GSK-3 β such as CaM kinase II, MAP kinase, Casein kinase, PKA, PKC and ROCK, but have a strong inhibitory activity on GSK-3 β . Therefore, the compounds of the present invention have a GSK-3 β -selective inhibitory activity and can be medicaments with small side-effect for diabetes, diabetic complications and neurodegenerative diseases (Alzheimer's disease, ischemic

cerebrovascular disorders, Down's syndrome, cerebral ischemia due to cerebral amyloid angiopathy, progressive supranuclear paralysis, subacute sclerosing panencephalitic Parkinsonism, postencephalitic Parkinsonism, boxer's encephalopathy, 5 Parkinsonism dementia complex of Guam, Lewy body disease, Pick's disease, corticobasal degeneration, frontotemporal dementia, AIDS encephalopathy, Huntington's disease, manic-depressive psychosis and the like). In addition, the compounds of the present invention are useful as immunopotentiators.

10 Formulations comprising the compounds of the present invention or salts thereof as an active ingredient are prepared using carriers, excipients and other additives conventionally used for formulation. The carrier and excipient for formulation may be a solid or liquid, and 15 include, for example, lactose, magnesium stearate, starch, talc, gelatin, agar, pectin, gum Arabic, olive oil, sesame oil, cacao butter, ethylene glycol and other conventionally used substances. Administration may be oral administration of tablet, pill, capsule, granule, powder, solution and the like, 20 or parenteral administration of injection (intravenous injection, intramuscular injection and the like), suppository, transdermal agent and the like. While the dose is appropriately determined on each case in consideration of symptom, age and sex of the administration subject, and the 25 like, it is generally 1 - 1,000 mg, preferably 50 - 200 mg per day for an adult person, which is orally administered once to several times a day, or 1 - 500 mg per day for an adult person, which is intravenously administered once to several times a day, or continuously administered intravenously for 1 to 24 30 hours a day.

As solid compositions for oral administration according to the present invention, tablet, powder, granule and the like are used. In such a solid composition, one or more active

substances are mixed with at least one inert diluent, such as lactose, mannitol, glucose, hydroxypropylcellulose, microcrystalline cellulose, starch, polyvinylpyrrolidone, metasilicic acid and magnesium aluminate. The composition may contain, according to a conventional method, inert additives other than diluent, for example, a lubricant such as magnesium stearate, a disintegrator such as cellulose and calcium glycolate, a stabilizer such as lactose and a solubilizer such as glutamic acid and aspartic acid. Tablet and pill may be coated with a gastric or enteric coating film of, for example, sucrose, gelatin, hydroxypropylcellulose and the like. Liquid compositions for oral administration include pharmaceutically acceptable emulsion, solution, suspension, syrup, elixir and the like, and contain an inert diluent generally used, such as purified water and ethanol. This composition may contain an adjuvant such as wetting agent and suspending agent, a sweetener, a flavor, an aromatic and an antiseptic, in addition to the inert diluent. Injections for parenteral administration contain sterile aqueous or non-aqueous solution, suspension and emulsion. The aqueous solution and suspension include, for example, propylene glycol, polyethylene glycol, vegetable oil such as olive oil, alcohols such as ethanol, polysorbate 80 and the like. Such a composition may contain adjuvants such as antiseptic, wetting agent, emulsifier, dispersant, stabilizer and solubilizer. These are sterilized by, for example, filtration through a bacteria-retaining filter, addition of an antimicrobial agent, irradiation of ultraviolet ray and the like. Alternatively, a sterile solid composition may be prepared and used upon dissolution in sterile water or sterile solvent for injection prior to use.

Examples

The present invention is described in detail in the following, based on Examples, Formulation Examples and

Experimental Examples. The scope of the present invention is not limited to these examples.

Example 1

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-
5 b]pyridine-5-carboxylate

A solution of 2-chlorobenzaldehyde (1.7 g), 3-aminopyrazole (1.0 g) and ethyl acetoacetate (1.6 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature and the
10 solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane- ethyl acetate (8:2)) to give the title compound (850 mg) as colorless crystals.

Melting Point (MP): 217-221°C.

15 Anal. Calcd. for: $C_{16}H_{16}N_3O_2Cl$: C, 60.47; H, 5.08; N, 13.22.

Found: C, 60.15; H, 5.07; N, 13.53.

MS (EI): 317 (M⁺).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.00 (3H, t, J=6.8Hz), 2.25 (3H, s),
3.72-3.82 (2H, m), 5.57 (1H, s), 7.07-7.12 (2H, m),
20 7.18 (1H, d, J=7.3Hz), 7.26 (1H, s), 7.34 (1H, d, J=7.9Hz),
9.53 (1H, br. s), 11.98 (1H, br. s).

IR (KBr): ν =3393, 3267, 1670, 1589, 1518, 1278, 1217 cm^{-1} .

Example 2

Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-methyl-2H-
25 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl acetoacetate in the same manner as in Example 1.

MP: 196-200°C.

30 Anal. Calcd. for: $C_{17}H_{19}N_3O$ 1/5 H_2O : C, 64.42; H, 6.17; N, 13.26.

Found: C, 64.08; H, 6.05; N, 13.68.

MS (EI): 313 (M⁺).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.00 (3H, t, J=6.8Hz), 2.81 (3H, s),

3.72 (3H, s), 3.87 (2H, q, J=6.8 Hz), 5.54 (1H, s), 6.80 (1H, dd, J=7.3 Hz and 7.4 Hz), 6.90 (1H, d, J=7.8 Hz), 7.04 (1H, d, J=7.4 Hz), 7.13-7.15 (2H, m), 9.99 (1H, br. s), 11.98 (1H, br. s).

IR(KBr): ν =3362, 3267, 3204, 3090, 1662, 1589, 1516, 1275, 1097 cm^{-1} .

5 Example 3

Ethyl 4,7-dihydro-6-methyl-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl acetoacetate in the same manner as in Example 1.

MP: 259-262°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{16}\text{F}_3\text{N}_3\text{O}_2 \cdot 1/5 \text{H}_2\text{O}$: C, 57.53; H, 4.66; N, 11.84.

Found: C, 57.56; H, 4.68; N, 11.86.

MS(EI): 352 ($\text{M}^+ + 1$).

^1H -NMR (400 MHz, $\text{DMSO}-d_6$) δ (ppm): 0.74 (3H, t, J=6.9 Hz), 2.40 (3H, s), 3.68-3.81 (2H, m), 5.42 (1H, s), 7.00 (1H, s), 7.28 (1H, dd, J=7.3 Hz and 7.4 Hz), 7.33 (1H, d, J=7.2 Hz), 7.51 (1H, dd, J=7.3 Hz and 7.4 Hz), 7.60 (1H, d, J=7.8 Hz), 9.58 (1H, br. s), 12.00 (1H, br. s).

IR(KBr): ν =3277, 3209, 3094, 1668, 1593, 1514, 1313, 1213, 1153, 1097, 765 cm^{-1} .

Example 4

Methyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and methyl acetoacetate in the same manner as in Example 1.

MP: 235°C.

Anal. Calcd. for: $\text{C}_{15}\text{H}_{14}\text{ClN}_3\text{O}_2 \cdot 2/5 \text{H}_2\text{O}$: C, 57.94; H, 4.80; N, 13.51.

Found: C, 58.03; H, 4.55; N, 13.43.

MS(EI): 303 (M^+).

^1H -NMR (400 MHz, $\text{DMSO}-d_6$) δ (ppm): 2.40 (3H, s), 3.34 (3H, s), 5.55 (1H, s), 7.09-7.11 (2H, m), 7.18 (1H, dd, J=7.3 Hz and 7.4 Hz), 7.29 (1H, s), 7.34 (1H, d, J=7.3 Hz), 9.57 (1H, br. s), 12.00 (1H, br. s).

Example 5

t-Butyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and t-butyl acetoacetate in the same manner as in Example 1.

MP:207°C.

Anal. Calcd. for: C₁₈H₂₀ClN₃O₂: C, 62.52; H, 5.83; N, 12.15.

Found: C, 62.51; H, 5.79; N, 12.17.

10 MS(EI): 345(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.07(9H, s), 2.36(3H, s), 5.50(1H, s), 7.11-7.15(2H, m), 7.20(1H, d, J=7.3Hz), 7.25(1H, s), 7.37(1H, d, J=7.3Hz), 9.35(1H, br.s), 11.93(1H, br.s).

Example 6

15 Isopropyl 4-(2-fluorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and isopropyl acetoacetate in the same manner as in Example 1.

20 MP:218-220°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.66(3H, d, J=6.3Hz), 1.02(3H, d, J=6.3Hz), 2.37(3H, s), 4.66(1H, q, J=6.3Hz), 5.40(1H, s), 7.01-7.14(4H, m), 7.19(1H, s), 9.46(1H, br.s), 11.97(1H, br.s).

Example 7

25 Benzyl 4-(2-chlorophenyl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and benzyl acetoacetate in the same manner as in Example 1.

30 MP:234°C.

Anal. Calcd. for: C₂₁H₁₈ClN₃O₂: C, 66.40; H, 4.78; N, 11.06.

Found: C, 66.16; H, 4.86; N, 10.92.

MS(EI): 379(M⁺).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 2.43(3H, s), 4.81(1H, d, $J=12.6\text{Hz}$), 4.92(1H, d, $J=12.6\text{Hz}$), 5.62(1H, s), 6.86-6.88(2H, m), 7.13-7.18(6H, m), 7.31-7.34(2H, m), 9.65(1H, br. s), 12.01(1H, br. s).

Example 8

5 4-(2-Chlorophenyl)-5-dimethylaminocarbonyl-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and N,N-dimethylacetamide in the same manner as in Example 1.

10 MP: 229°C.

Anal. Calcd. for: $\text{C}_{16}\text{H}_{17}\text{ClN}_4\text{O} \cdot 1/2 \text{H}_2\text{O}$: C, 58.99; H, 5.57; N, 17.20.

Found: C, 58.90; H, 5.46; N, 16.84.

MS(EI): 316(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.77(3H, s), 2.72(6H, s),
15 5.39(1H, s), 7.10-7.22(4H, m), 7.30(1H, d, $J=7.3\text{Hz}$), 8.40(1H, br. s), 11.83(1H, br. s).

Example 9

4-(2-Chlorophenyl)-5-hydrazinocarbonyl-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine

20 To a solution of 4-(2-chlorophenyl)-4,7-dihydro-5-dimethylaminocarbonyl-6-methyl-2H-pyrazolo[3,4-b]pyridine (200 mg) in acetonitrile (200 mL) was added hydrazine (200 mg) and the mixture was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated
25 crystals were collected by filtration and washed with ethyl acetate to give the title compound as colorless crystals (150 mg).

MP: 220°C.

Anal. Calcd. for: $\text{C}_{14}\text{H}_{14}\text{ClN}_5\text{O} \cdot 3/10 \text{H}_2\text{O}$: C, 54.39; H, 4.76; N, 22.65.

30 Found: C, 54.36; H, 4.56; N, 22.65.

MS(EI): 303(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.85(3H, s), 3.20-3.80(3H, br. s), 5.15(1H, s), 6.81(1H, s), 7.16-7.028(3H, m), 7.34(1H, d, $J=7.3\text{Hz}$),

10.05-11.07(2H,brs).

Example 10

4-(2-Fluorophenyl)-4,7-dihydro-6-methyl-5-isopropylthiocarbonyl-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and acetoacetic acid isopropyl thioester in the same manner as in Example 1.
MP:192-194°C.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 1.03(3H,d,J=6.9Hz),
10 1.15(3H,d,J=6.9Hz), 2.43(3H,s), 3.35(1H,q,J=6.9Hz), 5.55(1H,s),
7.04-7.15(4H,m), 7.33(1H,s), 9.81(1H,br.s), 12.11(1H,br.s).

Example 11

4,7-Dihydro-6-methyl-5-nitro-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and 1-nitropropan-2-one in the same manner as in Example 1.
MP:257-258°C.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 2.65(3H,s), 5.75(1H,s),
20 7.19(1H,s), 7.30-7.35(2H,m), 7.51(1H,dd,J=7.3Hz and 7.8Hz),
7.66(1H,d,J=7.8Hz), 10.87(1H,br.s), 12.45(1H,br.s).

Example 12

Ethyl 4,7-dihydro-4-phenyl-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

25 The title compound was prepared from benzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:110-115°C.

Anal. Calcd. for:C₁₆H₁₄N₃O₂F₃ 1/2 H₂O:C,55.49;H,4.37;N,12.13.

30 Found:C,55.84;H,4.70;N,11.89.

MS(EI):337(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.84(3H,t,J=6.9Hz),
3.90(2H,q,J=6.8Hz), 5.54(1H,s), 7.13-7.17(3H,m), 7.24-

7.28(3H,m), 9.78(1H,br.s), 12.20(1H,br.s).

IR(KBr): ν =3375,3175,3067,1707,1606,1533,1278,1206,1197,1167 cm^{-1} .

Example 13

Ethyl 4-(2-fluorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-
5 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-fluorobenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:119-120°C.

10 Anal. Calcd. for: $\text{C}_{16}\text{H}_{13}\text{F}_4\text{N}_3\text{O}_2$: C, 54.09; H, 3.69; N, 11.84.

Found: C, 53.84; H, 3.57; N, 11.79.

MS(EI): 356(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.94 (3H,t, J=6.8Hz),
3.89(2H,q, J=6.8Hz), 5.46(1H,s), 7.11-7.20(4H,m), 7.28-

15 7.30(1H,m), 9.92(1H,br.s), 12.27(1H,br.s).

IR(KBr): ν =3290,3178,3069,1703,1608,1537,1280,1232,1174,1138,
756 cm^{-1} .

Example 14

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-
20 pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:171-172°C.

25 MS(EI): 371(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.91 (3H,t, J=7.3Hz),
3.50(3H,br.s), 3.87 (2H,q, J=6.8Hz), 5.66(1H,s), 6.26(2H,s),
7.15-7.18(2H,m), 7.27(1H,d, J=7.8Hz), 7.30(1H,s),
7.40(1H,d, J=7.8Hz), 9.65(1H,br.s).

30 IR(KBr): ν =3297,2935,1730,1624,1550,1479,1186 cm^{-1} .

Example 15

Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-trifluoromethyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:144-146°C.

5 Anal. Calcd. for: $C_{17}H_{16}F_3N_3O_3$: C, 55.59; H, 4.39; N, 11.44.

Found: C, 55.55; H, 4.38; N, 11.43.

MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94(3H, t, J=6.8Hz), 3.83(3H, s),
3.89(2H, q, J=6.8Hz), 5.51(1H, s), 6.84(1H, dd, J=7.3Hz and 7.4Hz),
10 6.94-6.97(2H, m), 7.13(1H, dd, J=7.3Hz and 7.4Hz), 7.20(1H, s),
9.70(1H, br.s), 12.13(1H, br.s).

IR(KBr): ν =3431, 3173, 3067, 2993, 2924, 1689, 1610, 1527, 1286, 1226,
1145 cm^{-1} .

Example 16

15 Ethyl 4,7-dihydro-6-trifluoromethyl-4-(2-trifluoromethylphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl
20 trifluoroacetoacetate in the same manner as in Example 1.

MP:182-186°C.

Anal. Calcd. for: $C_{17}H_{13}N_3O_2F_6$: C, 50.38; H, 3.23; N, 10.37.

Found: C, 50.21; H, 3.15; N, 10.39.

MS(FAB): 406 (M^++1).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.83 (3H, t, J=6.8Hz),
3.83(2H, q, J=6.8Hz), 5.49(1H, s), 7.08(1H, s), 7.35-7.39(2H, m),
7.62(1H, dd, J=7.3Hz and 7.4Hz), 7.66(1H, d, J=7.8Hz),
9.97(1H, br.s), 12.30(1H, br.s).

IR(KBr): ν =3339, 3177, 3067, 1711, 1608, 1537, 1313, 1280, 1182, 1141 cm^{-1} .

30 Example 17

Ethyl 4-(3-chlorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3-

chlorobenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:144-145°C.

Anal. Calcd. for: $C_{16}H_{13}N_3O_2F_3Cl$: C, 51.69; H, 3.52; N, 11.30.

5 Found: C, 51.33; H, 3.74; N, 11.10.

MS(EI): 371(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.98 (3H, t, J=6.8Hz),
3.92(2H, q, J=6.8Hz), 5.21(1H, s), 7.11(1H, d, J=7.8Hz), 7.17(1H, s),
7.23(1H, d, J=8.7Hz), 7.29-7.33(2H, m), 9.92(1H, br. s),

10 12.30(1H, br. s).

IR(KBr): ν =3321, 3178, 3070, 1703, 1610, 1535, 1278, 1224, 1184, 1145 cm^{-1} .

Example 18

Ethyl 4-(4-chlorophenyl)-4,7-dihydro-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from 4-chlorobenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:176-178°C.

Anal. Calcd. for: $C_{16}H_{13}F_3N_3O_2Cl$: C, 51.69; H, 3.52; N, 11.30.

20 Found: C, 51.91; H, 3.77; N, 11.08.

MS(EI): 371(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.98 (3H, t, J=6.8Hz),
3.90(2H, q, J=7.3Hz), 5.92(1H, s), 7.16(2H, d, J=8.2Hz), 7.27(1H, s),
7.31(2H, d, J=8.2Hz), 9.87(1H, br. s), 12.27(1H, br. s).

25 IR(KBr): ν =3476, 3368, 3178, 3078, 1714, 1695, 1606, 1537, 1278, 1172, 1134 cm^{-1} .

Example 19

Ethyl 4,7-dihydro-4-(4-methoxyphenyl)-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 4-methoxybenzaldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in the same manner as in Example 1.

MP:159-161°C.

Anal. Calcd. for: $C_{17}H_{16}FN_3O_3$: C, 55.59; H, 4.39; N, 11.44.

Found: C, 55.49; H, 4.54; N, 11.33.

MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.99 (3H, t, $J=7.3$ Hz), 3.68 (3H, s),
5 3.89 (2H, q, $J=7.3$ Hz), 5.12 (1H, s), 6.82 (2H, d, $J=8.7$ Hz),
7.03 (2H, d, $J=8.7$ Hz), 7.22-7.24 (1H, m), 9.71 (1H, br. s),
12.19 (1H, br. s).

IR(KBr): $\nu=3323, 3231, 3173, 3067, 1699, 1610, 1535, 1510, 1302, 1248, 1184, 1145$ cm $^{-1}$.

10 Example 20

Ethyl 4-(4-ethoxycarbonylphenyl)-4,7-dihydro-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 4-ethoxycarbonylbenzaldehyde, 3-aminopyrazole and ethyl
15 trifluoroacetoacetate in the same manner as in Example 1.
MP: 157-160°C.

Anal. Calcd. for: $C_{19}H_{18}F_3N_3O_4$: C, 55.75; H, 4.43; N, 10.26.

Found: C, 55.68; H, 4.39; N, 10.43.

MS(FAB): 410 ($M^+ + 1$).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.96 (3H, t, $J=6.9$ Hz), 1.28
(3H, t, $J=7.3$ Hz), 3.89 (2H, q, $J=6.8$ Hz), 4.27 (2H, q, $J=7.3$ Hz),
5.28 (1H, s), 7.27 (1H, s), 7.29 (2H, d, $J=8.3$ Hz), 7.87 (2H, d, $J=8.2$ Hz),
9.92 (1H, br. s), 12.28 (1H, br. s).

IR(KBr): $\nu=3393, 3188, 3082, 1692, 1612, 1539, 1284$ cm $^{-1}$.

25 Example 21

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-3-methyl-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-amino-5-methylpyrazole and ethyl
30 trifluoroacetoacetate in the same manner as in Example 1.
MP: 165-168°C.

MS(EI): 385 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94 (3H, t, $J=7.3$ Hz), 1.81 (3H, s),

3.85(2H,q,J=6.8Hz), 5.54(1H,s), 7.17-7.20(2H,m),
7.27(1H,dd,J=7.3Hz and 7.4Hz), 7.36(1H,d,J=8.3Hz),
9.79(1H,br.s), 11.96(1H,br.s).
IR(KBr): ν =3263,3194,3080,1668,1591,1520,1286,1232,1149,1095,
5 1062 cm^{-1} .

Example 22

Ethyl 4,7-dihydro-4-(thiophen-2-yl)-6-trifluoromethyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from thiophene-2-
10 aldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in
the same manner as in Example 1.

MP:157-161°C.

Anal. Calcd. for: $\text{C}_{14}\text{H}_{12}\text{F}_3\text{N}_3\text{O}_2\text{S}$: C, 49.27; H, 2.95; N, 12.31.

Found: C, 49.10; H, 3.28; N, 12.13.

15 MS(EI): 343(M^+).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.08 (3H,t,J=7.4Hz), 4.00
(2H,q,J=7.4Hz), 5.52(1H,s), 6.76(1H,d,J=2.9Hz),
6.87(1H,dd,J=2.9Hz and 5.4Hz), 7.30(1H,d,J=5.4Hz), 7.43(1H,s),
9.96(1H,br.s), 12.35(1H,br.s).

20 IR(KBr): ν =3350,3240,3180,1693,1612,1535,1396,1371,1304,1153,109
3,1057,694 cm^{-1} .

Example 23

Ethyl 4,7-dihydro-4-(thiophen-3-yl)-6-trifluoromethyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

25 The title compound was prepared from thiophene-3-
aldehyde, 3-aminopyrazole and ethyl trifluoroacetoacetate in
the same manner as in Example 1.

MP:140-145°C.

Anal. Calcd. for: $\text{C}_{14}\text{H}_{12}\text{F}_3\text{N}_3\text{O}_2\text{S}$: C, 49.27; H, 2.95; N, 12.31.

30 Found: C, 49.65; H, 2.64; N, 12.19.

MS(EI): 343(M^+).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.03 (3H,t,J=7.3Hz), 3.96
(2H,q,J=7.3Hz), 5.30(1H,s), 6.87(1H,d,J=4.8Hz), 7.05(1H,s),

7.35(1H,s), 7.39(1H,dd,J=2.9Hz and 4.8Hz), 9.76(1H,br.s),
12.25(1H,br.s).

IR(KBr): ν =3356,3182,2982,2932,1689,1614,1537,1304,1224,1153 cm^{-1} .

Example 24

5 Ethyl 4,7-dihydro-4-(1-naphthyl)-6-trifluoromethyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from naphthalene-1-aldehyde, 3-aminopyrazole and ethyl trifluoroacetate in the same manner as in Example 1.

10 MP:119-120°C.

Anal. Calcd. for: $\text{C}_{20}\text{H}_{16}\text{F}_3\text{N}_3\text{O}_2 \cdot 1/2 \text{H}_2\text{O}$:C,60.45;H,4.57;N,10.57.

Found:C,60.20;H,4.77;N,10.39.

MS(FAB):388(M^+ +1).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.69 (3H,t,J=6.8Hz),

15 3.73(2H,q,J=6.8Hz), 6.04(1H,s), 7.09(1H,s), 7.26(1H,d,J=6.8Hz),
7.41(1H,dd,J=7.3Hz and 7.4Hz), 7.52-7.58(2H,m),
7.75(1H,d,J=8.3Hz), 7.92(1H,dd,J=7.3Hz and 7.4Hz), 8.33(1H,s),
9.87(1H,br.s), 12.14(1H,br.s).

IR(KBr): ν =3173,1670,1606,1138,1095 cm^{-1} .

20 Example 25

Ethyl 4,7-dihydro-4-phenyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

A solution of benzaldehyde (1.6 g), 3-aminopyrazole (1.0 g) and ethyl 3-ketohexanoate (1.9 g) in acetonitrile (20 mL)
25 was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (720 mg) as colorless
30 crystals.

MP:139-141°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{21}\text{N}_3\text{O}_2\text{C}_4\text{H}_4\text{O}_4 \cdot 1/2 \text{H}_2\text{O}$:C,60.54;H,6.00;N,9.63.

Found: C,60.16;H,5.60;N,10.01.

MS(EI):311(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.94-0.95 (6H,m), 1.62
(2H,q,J=7.8Hz), 2.66-2.77(2H,m), 3.50(3H,br.s),
3.83(2H,q,J=6.8Hz), 5.10(1H,s), 6.25(2H,s), 7.05-7.20(6H,m),
5 9.37(1H,br.s).

IR(KBr): ν =3337,3042,1699,1593,1467,1539,1361,1203 cm^{-1}

Example 26

Ethyl 4-(2-fluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

10 The title compound was prepared from 2-
fluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
in the same manner as in Example 25.

MP:192-194°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{20}\text{FN}_3\text{O}_2$ 1/2 H_2O :C,63.89;H,6.26;N,12.42.

15 Found:C,63.85;H,6.01;N,12.36.

MS(EI):329(M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.93 (3H,t,J=7.3Hz), 0.97
(3H,t,J=7.3Hz), 1.62-1.68(2H,m), 2.71-2.83(2H,m),
3.82(2H,q,J=7.3Hz), 5.43(1H,s), 7.05-7.11(4H,m), 7.21(1H,s),
20 9.48(1H,br.s), 11.97(1H,br.s).

IR(KBr): ν =3265,3198,2964,1591,1514,1224,1209,1093 cm^{-1} .

Example 27

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

25 The title compound was prepared from 2-
chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
in the same manner as in Example 25.

MP:202-205°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{20}\text{ClN}_3\text{O}_2$:C,62.52;H,5.83;N,12.15.

30 Found:C,62.28;H,5.76;N,12.37.

MS(FAB):346(M^++1).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.85 (3H,t,J=6.8Hz), 0.95
(3H,t,J=7.3Hz), 1.62-1.68(2H,m), 2.67-2.87(2H,m),

3.78(2H,q,J=6.8Hz), 5.58(1H,s), 7.07-7.11(2H,m),
7.18(1H,dd,J=7.3Hz and 7.4Hz), 7.25(1H,s), 7.34(1H,d,J=7.8Hz),
9.49(1H,br.s), 11.97(1H,br.s).

IR(KBr): ν =3263,3209,3194,3080,1668,1591,1520,1286,1232,1149,106
5 2,750 cm^{-1} .

Example 28

Methyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-
10 chlorobenzaldehyde, 3-aminopyrazole and methyl 3-ketohexanoate
in the same manner as in Example 25.

MP:203-207°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{18}\text{ClN}_3\text{O}_2$ 1/5 H_2O :C,60.88;H,5.53;N,12.53.

Found:C,60.73;H,5.36;N,12.14.

15 MS(EI):331(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.97 (3H,t,J=7.3Hz), 1.64-
1.66(2H,m), 2.72-2.83(2H,m), 3.31(3H,s), 5.57(1H,s),
7.10(1H,d,J=7.3Hz), 7.09-7.11(1H,m), 7.17-7.18(1H,m),
7.27(1H,s), 7.34(1H,d,J=7.8Hz), 9.54(1H,br.s), 11.97(1H,br.s).

20 IR(KBr): ν =3260,3190,1672,1591,1516,1232 cm^{-1} .

Example 29

Ethyl 4-(2-bromophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-bromobenzaldehyde,
25 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner
as in Example 25.

MP:223°C.

Anal. Calcd. for: $\text{C}_{18}\text{H}_{20}\text{BrN}_3\text{O}_2$:C,55.40;H,5.17;N,10.77.

Found:C,55.08;H,5.14;N,10.85.

30 MS(EI):390(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.86(3H,t,J=7.3Hz),
0.97(3H,t,J=7.3Hz), 1.63-1.69(2H,m), 2.71-2.74(1H,m), 2.80-
2.83(1H,m), 3.77(2H,q,J=7.3Hz), 5.67(1H,s), 7.00(1H,dd,J=7.3Hz

and 7.4Hz), 7.10(1H,d,J=7.3Hz), 7.22(1H,dd,J=7.3Hz and 7.4Hz), 7.28(1H,s), 7.51(1H,d,J=7.3Hz), 9.50(1H,br.s), 11.97(1H,br.s).

Example 30

Ethyl 4,7-dihydro-4-(2-methylphenyl)-6-propyl-2H-pyrazolo[3,4-
5 b]pyridine-5-carboxylate

The title compound was prepared from 2-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:178°C.

10 Anal. Calcd. for: C₁₉H₂₃N₃O₂: C, 70.13; H, 7.12; N, 12.91.

Found: C, 70.12; H, 7.35; N, 12.99.

MS(EI): 325(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.83(3H,t,J=7.3Hz),
0.96(3H,t,J=7.3Hz), 1.62-1.66(2H,m), 2.44(3H,s), 2.64-
15 2.66(1H,m), 2.76-2.79(1H,m), 3.77(2H,q,J=7.3Hz), 5.31(1H,s),
6.93(1H,d,J=7.3Hz), 6.99-7.05(3H,m), 7.18(1H,s), 9.34(1H,br.s),
11.87(1H,br.s).

Example 31

Ethyl 4,7-dihydro-6-propyl-4-(2-trifluoromethylphenyl)-2H-
20 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:198-202°C.

25 Anal. Calcd. for: C₁₉H₂₀F₃N₃O₂ 1/2 H₂O: C, 58.76; H, 5.45; N, 10.81.

Found: C, 58.82; H, 5.92; N, 10.62.

MS(EI): 379(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.76 (3H,t,J=7.3Hz),
0.98(3H,t,J=7.3Hz), 1.64-1.68(2H,m), 2.76-2.79(2H,m),
30 3.80(2H,q,J=7.3Hz), 5.44(1H,s), 7.00(1H,s), 7.27-7.30(1H,m),
7.33(1H,d,J=7.8Hz), 7.53(1H,dd,J=7.3Hz and 7.4Hz),
7.61(1H,d,J=7.3Hz), 9.54(1H,br.s), 11.99(1H,br.s).

IR(KBr): ν=3265, 3198, 2964, 1591, 1514, 1224, 1209, 1093cm⁻¹.

Example 32Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:169°C.

Anal. Calcd. for: C₁₉H₂₃N₃O₃: C, 66.84; H, 6.79; N, 12.31.

Found: C, 66.58; H, 6.50; N, 12.34.

10 MS(EI): 341(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.66-1.68(2H, m), 2.66-2.70(1H, m), 2.81-
2.88(1H, m), 3.80(2H, q, J=7.3Hz), 3.85(3H, s), 5.47(1H, s),
6.76(1H, dd, J=7.3Hz and 7.4Hz), 6.89-6.94(2H, m),
15 7.04(1H, dd, J=7.3Hz and 7.4Hz), 7.14(1H, s), 9.29(1H, br.s),
11.82(1H, br.s).

Example 33Ethyl 4-(2-ethoxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was prepared from 2-ethoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:203°C.

Anal. Calcd. for: C₂₀H₂₅N₃O₃: C, 67.58; H, 7.09; N, 11.82.

25 Found: C, 67.48; H, 7.06; N, 11.81.

MS(EI): 355(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.41(3H, t, J=7.3Hz), 1.64-1.67(2H, m), 2.68-
2.71(1H, m), 2.78-2.81(1H, m), 3.79(2H, q, J=7.3Hz), 4.03-
30 4.05(1H, m), 4.10-4.12(1H, m), 5.48(1H, s), 6.74(1H, dd, J=7.3Hz
and 7.4Hz), 6.87(1H, d, J=7.3Hz), 6.94(1H, d, J=7.3Hz),
7.01(1H, dd, J=7.3Hz and 7.4Hz), 7.14(1H, s), 9.28(1H, br.s),
11.79(1H, br.s).

Example 34

Ethyl 4,7-dihydro-4-(2-propoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-propoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:205°C.

Anal. Calcd. for: C₂₁H₂₇N₃O₃: C, 68.27; H, 7.37; N, 11.37.

Found: C, 68.05; H, 7.39; N, 11.35.

10 MS(EI): 369 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.3Hz), 0.97(3H, t, J=7.3Hz), 1.05(3H, t, J=7.3Hz), 1.64-1.67(2H, m), 1.81-1.84(2H, m), 2.70-2.73(1H, m), 2.78-2.82(1H, m), 3.77(2H, q, J=7.3Hz), 3.92(1H, q, J=7.3Hz), 4.07(1H, q, J=7.3Hz), 15 5.52(1H, s), 6.75(1H, dd, J=7.3Hz and 7.4Hz), 6.88(1H, d, J=7.3Hz), 6.94(1H, d, J=7.3Hz), 7.01(1H, dd, J=7.3Hz and 7.4Hz), 7.11(1H, s), 9.28(1H, br.s), 11.79(1H, br.s).

Example 35

Ethyl 4,7-dihydro-4-(2-isopropoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-isopropoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:210°C.

25 Anal. Calcd. for: C₂₁H₂₇N₃O₃: C, 68.27; H, 7.37; N, 11.37.

Found: C, 67.93; H, 7.39; N, 11.32.

MS(EI): 369 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.3Hz), 0.97(3H, t, J=7.3Hz), 1.25(3H, d, J=6.8Hz), 1.39(3H, d, J=6.8Hz), 30 1.64-1.69(2H, m), 2.68-2.72(1H, m), 2.78-2.82(1H, m), 3.77(2H, q, J=7.3Hz), 4.64-4.67(1H, m), 5.45(1H, s), 6.73(1H, dd, J=7.3Hz and 7.4Hz), 6.89-6.90(3H, m), 7.15(1H, s), 9.27(1H, br.s), 11.77(1H, br.s).

Example 36

Ethyl 4-(2-butoxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-butoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:171°C.

Anal. Calcd. for: C₂₂H₂₉N₃O₃: C, 68.90; H, 7.62; N, 10.96.

Found: C, 68.66; H, 7.63; N, 10.89.

MS(EI): 383(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.3Hz), 0.95-0.99(6H, m), 1.52-1.80(6H, m), 2.69-2.71(1H, m), 1.76-1.80(1H, m), 3.77(2H, q, J=7.3Hz), 3.95-3.98(1H, m), 4.07-4.10(1H, m), 5.51(1H, s), 6.74(1H, dd, J=7.3Hz and 7.4Hz), 6.88-6.94(2H, m), 7.01(1H, dd, J=7.3Hz and 7.4Hz), 7.10(1H, s), 9.28(1H, br.s), 11.79(1H, br.s).

Example 37

Ethyl 4-(2-cyclopentyloxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-cyclopentyloxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:195°C.

Anal. Calcd. for: C₂₃H₂₉N₃O₃: C, 69.85; H, 7.39; N, 10.62.

Found: C, 69.63; H, 7.28; N, 10.61.

MS(EI): 395(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.83(3H, t, J=7.3Hz), 0.97(3H, t, J=7.3Hz), 1.65-1.98(8H, m), 2.66-2.78(2H, m), 3.76(2H, q, J=7.3Hz), 4.89-4.93(1H, m), 5.43(1H, s), 6.72(1H, dd, J=7.3Hz and 7.4Hz), 6.88-6.93(2H, m), 7.00(1H, dd, J=7.3Hz and 7.4Hz), 7.10(1H, s), 9.28(1H, br.s), 11.77(1H, br.s).

Example 38

Ethyl 4-(2-benzyloxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-benzyloxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:128°C.

Anal. Calcd. for: C₂₅H₂₇N₃O₃: C, 71.92; H, 6.52; N, 10.06.

Found: C, 71.66; H, 6.73; N, 9.85.

MS(EI): 417(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.3Hz), 0.97(3H, t, J=7.3Hz), 1.64-1.67(2H, m), 2.70-2.73(1H, m), 2.80-2.83(1H, m), 3.80(2H, q, J=7.3Hz), 5.20(2H, d, J=30Hz), 5.60(1H, s), 6.78(1H, dd, J=7.3Hz and 7.4Hz), 6.96-7.03(3H, m), 7.08(1H, s), 7.35(1H, dd, J=7.3Hz and 7.4Hz), 7.40-7.43(2H, m), 7.52-7.55(2H, m), 9.30(1H, br.s), 11.79(1H, br.s).

Example 39

Ethyl 4,7-dihydro-4-(2-methylthiophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of 2-methylthiobenzaldehyde (20 g), Meldrum's acid (19 g), ethyl 3-ketohexanoate (21 g) and ammonium acetate (11 g) in acetic acid (130 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give colorless crystals (9.7 g). To a solution of dimethylformamide (1.3 g) in chloroform (5 mL) were added phosphorus oxychloride (1.7 mL) and a solution of the obtained colorless crystals (1.5 g) in chloroform (10 mL) under ice-cooling, and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (18.5 g) solution was added and the mixture was stirred for one hour. The reaction mixture was extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate

(8:2)) to give colorless crystals (0.9 g). To a solution of the obtained colorless crystals (0.9 g) in pyridine (10 mL) was added hydrazine (0.27 g) and the mixture was stirred with heating for 3 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (230 mg) as colorless crystals.

MP:198°C.

Anal. Calcd. for: $C_{19}H_{23}N_3O_2S$: C, 63.84; H, 6.49; N, 11.75.

Found: C, 63.56; H, 6.45; N, 11.64.

MS(EI): 357 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.82(3H, t, J=7.3Hz), 0.96(3H, t, J=7.3Hz), 1.62-1.68(2H, m), 2.48(3H, s), 2.67-2.71(1H, m), 2.79-2.83(1H, m), 3.74(2H, q, J=7.3Hz), 5.54(1H, s), 6.99-7.06(3H, m), 7.22-7.25(2H, m), 9.38(1H, br.s), 11.86(1H, br.s).

Example 40

Ethyl 4,7-dihydro-4-(2-methylsulfinylphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of ethyl 4,7-dihydro-4-(2-methylthio)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (100 mg) in tetrahydrofuran (3.0 mL) was added metachloroperbenzoic acid (60 mg) and the mixture was stirred at -78°C for 30 minutes. An aqueous sodium thiosulfate solution was added, and the mixture was extracted with chloroform. The solvent was evaporated under reduced pressure to give colorless crystals. By recrystallization from ethyl acetate, the title compound (50 mg) was obtained as colorless crystals.

MP:216°C.

Anal. Calcd. for: $C_{19}H_{23}N_3O_3S$: C, 61.10; H, 6.21; N, 11.25.

Found: C, 61.32; H, 6.18; N, 10.99.

MS(EI): 373 (M^+).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.91(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.64-1.68(2H, m), 2.69-2.72(1H, m),
2.72(3H, s), 2.76-2.79(1H, m), 3.90(2H, q, J=7.3Hz), 5.36(1H, s),
7.15(1H, dd, J=7.3Hz and 7.4Hz), 7.20(1H, s), 7.37-7.39(2H, m),
5 7.85(1H, dd, J=7.3Hz and 7.4Hz), 9.59(1H, br.s), 12.04(1H, br.s).

Example 41Ethyl 4,7-dihydro-4-(2-nitrophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-nitrobenzaldehyde
10 and ethyl 3-ketohexanoate in the same manner as in Example 39.
MP:218°C.

Anal. Calcd. for: C₁₈H₂₀N₄O₄: C, 60.66; H, 5.66; N, 15.72.

Found: C, 60.25; H, 5.65; N, 15.44.

MS(EI): 356(M⁺).

15 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.80(3H, t, J=7.3Hz),
0.95(3H, t, J=7.3Hz), 1.59-1.64(2H, m), 2.69-2.73(1H, m), 2.77-
2.80(1H, m), 3.72(2H, q, J=7.3Hz), 5.45(1H, s), 7.28-7.33(3H, m),
7.56(1H, dd, J=7.3Hz and 7.4Hz), 7.76(1H, d, J=7.3Hz),
9.64(1H, br.s), 10.07(1H, br.s).

20 Example 42Ethyl 4-(2-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-cyanobenzaldehyde
and ethyl 3-ketohexanoate in the same manner as in Example 39.
25 MP:211°C.

Anal. Calcd. for: C₁₉H₂₀N₄O₂: C, 67.84; H, 5.99; N, 16.66.

Found: C, 67.49; H, 6.14; N, 16.23.

MS(EI): 336(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.89(3H, t, J=7.3Hz),
30 0.94(3H, t, J=7.3Hz), 1.61-1.67(2H, m), 2.71-2.73(1H, m), 2.79-
2.82(1H, m), 3.80(2H, q, J=7.3Hz), 5.48(1H, s), 7.21-7.29(2H, m),
7.28(1H, dd, J=7.3Hz and 7.4Hz), 7.55(1H, dd, J=7.3Hz and 7.4Hz),
7.70(1H, d, J=7.3Hz), 9.63(1H, br.s), 12.07(1H, br.s).

Example 43Ethyl 4-(2,3-difluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-difluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:207°C.

Anal. Calcd. for: $C_{18}H_{19}F_2N_3O_2 \cdot 1/5 H_2O$: C, 61.60; H, 5.57; N, 11.97.

Found: C, 61.41; H, 5.56; N, 11.59.

10 MS(EI): 347(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90-0.97(6H, m), 1.60-1.66(2H, m), 2.68-2.71(1H, m), 2.79-2.82(1H, m), 3.83(2H, q, $J=7.3$ Hz), 5.45(1H, s), 6.87(1H, dd, $J=7.3$ Hz and 7.4Hz), 7.03-7.13(2H, m), 7.76(1H, s), 9.55(1H, br.s), 12.03(1H, br.s).

15 Example 44Ethyl 4-(2,3-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-dichlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:220°C.

Anal. Calcd. for: $C_{18}H_{19}Cl_2N_3O_2$: C, 56.85; H, 5.04; N, 11.05.

Found: C, 56.35; H, 5.00; N, 11.01.

MS(EI): 380(M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, $J=7.3$ Hz), 0.99(3H, t, $J=7.3$ Hz), 1.66-1.69(2H, m), 2.74-2.77(1H, m), 2.82-2.86(1H, m), 3.81(2H, q, $J=7.3$ Hz), 5.66(1H, s), 7.10(1H, d, $J=7.3$ Hz), 7.24(1H, dd, $J=7.3$ Hz and 7.4Hz), 7.31(1H, s), 7.38(1H, d, $J=7.3$ Hz), 9.59(1H, br.s), 12.04(1H, br.s).

30 Example 45Ethyl 4-(3-fluoro-2-methylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3-fluoro-2-

methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:159-162°C.

Anal. Calcd. for: C₁₉H₂₂FN₃O₃ 3/10 H₂O: C, 65.42; H, 6.53; N, 12.05.

5 Found: C, 65.56; H, 6.29; N, 12.40.

MS(EI): 343(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89 (3H, t, J=7.3Hz), 0.97 (3H, t, J=7.3Hz), 1.64(2H, m), 2.36(3H, s), 2.67-2.84(2H, m), 3.80(2H, q, J=7.3Hz), 5.35(1H, s), 6.86(2H, d, J=8.8Hz),
10 7.07(1H, dd, J=7.3Hz and 7.4Hz), 7.23(1H, s), 9.42(1H, br.s), 11.94(1H, br.s).

IR(KBr): ν=3265, 3193, 2966, 2934, 1668, 1591, 1520, 1466, 1240 cm⁻¹.

Example 46

Ethyl 4-(2,3-dimethoxyphenyl)-4,7-dihydro-6-propyl-2H-
15 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-dimethoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:205-206°C.

20 Anal. Calcd. for: C₂₀H₂₅N₃O₄: C, 64.67; H, 6.78; N, 11.31.

Found: C, 64.76; H, 6.81; N, 11.15.

MS(EI): 371(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90(3H, t, J=7.4Hz), 0.98(3H, t, J=7.3Hz), 1.66-1.68(2H, m), 2.68-2.70(1H, m), 2.80-
25 2.83(1H, m), 3.77(3H, s), 3.80(3H, s), 3.80-3.85(2H, m), 5.44(1H, s), 6.58(1H, d, J=7.3Hz), 6.76(1H, d, J=6.8Hz), 6.88(1H, dd, J=7.3Hz and 7.4Hz), 7.11(1H, s), 9.32(1H, br.s), 11.83(1H, br.s).

Example 47

30 Ethyl 4-(2-chloro-3-trifluoromethylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-3-trifluoromethylbenzaldehyde, 3-aminopyrazole and ethyl 3-

keto hexanoate in the same manner as in Example 25.

MP: 236-238°C.

Anal. Calcd. for: C₁₉H₁₉ClF₃N₃O₂: C, 55.15; H, 4.63; N, 10.15.

Found: C, 55.07; H, 4.55; N, 10.13.

5 MS(EI): 413(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.82(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.65(2H, m), 2.70-2.90(2H, m), 3.65-
3.85(2H, m), 5.72(1H, s), 7.29(1H, s), 7.41-7.42(2H, m), 7.59-
7.61(1H, m), 9.62(1H, br.s), 12.05(1H, br.s).

10 Example 48

Ethyl 4-(2-chloro-4-fluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-4-fluorobenzaldehyde, 3-aminopyrazole and ethyl 3-keto hexanoate

15 in the same manner as in Example 25.

MS(EI): 363(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H, t, J=7.3Hz),
0.96(3H, t, J=7.3Hz), 1.62-1.67(2H, m), 2.66-2.80(2H, m),
3.77(2H, q, J=7.3Hz), 5.54(1H, s), 7.08-7.13(2H, m), 7.25(1H, s),
20 7.32(1H, dd, J=2.5Hz and 8.8Hz), 9.53(1H, br.s), 11.99(1H, br.s).

Example 49

Ethyl 4-(2,5-difluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,5-difluorobenzaldehyde, 3-aminopyrazole and ethyl 3-keto hexanoate in the same manner as in Example 25.

MP: 168-169°C.

MS(EI): 347(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.92-0.99(6H, m), 1.62-1.68(2H, m),
30 2.67-2.71(1H, m), 2.85-2.88(1H, m), 3.80-3.91(2H, m),
4.03(1H, q, J=6.8Hz), 5.40(1H, s), 6.77-6.80(1H, m), 6.98-
7.00(1H, m), 7.12-7.16(1H, m), 7.26(1H, s), 9.59(1H, br.s),
12.06(1H, br.s).

Example 50Ethyl 4-(2,5-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,5-dichlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:162°C.

Anal. Calcd. for: $C_{18}H_{19}Cl_2N_3O_2 \cdot 1/2 H_2O$: C, 55.54; H, 5.18; N, 10.79.

Found: C, 55.50; H, 5.50; N, 11.17.

10 MS(EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=7.3Hz), 0.98(3H, t, J=7.3Hz), 1.62-1.66(2H, m), 2.64-2.67(1H, m), 2.86-2.90(1H, m), 3.81(2H, q, J=7.3Hz), 5.55(1H, s), 7.04(1H, s), 7.18(1H, d, J=7.3Hz), 7.28(1H, s), 7.41(1H, d, J=7.3Hz),

15 9.61(1H, br.s), 12.06(1H, br.s).

Example 51Ethyl 4-(5-fluoro-2-methoxyphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 5-fluoro-2-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:164-167°C.

Anal. Calcd. for: $C_{19}H_{22}FN_3O_3$: C, 63.50; H, 6.17; N, 11.69.

Found: C, 63.24; H, 6.09; N, 11.70.

25 MS(EI): 359 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87(3H, t, J=7.3Hz), 0.98(3H, t, J=7.3Hz), 1.64-1.69(2H, m), 2.62-2.91(2H, m), 3.79(2H, q, J=7.3Hz), 3.85(3H, s), 5.44(1H, s), 6.33(1H, dd, J=3.0Hz and 7.8Hz), 6.83-6.91(2H, m), 7.17(1H, s), 9.41(1H, br.s),

30 11.89(1H, br.s).

IR(KBr): ν =3252, 2955, 1657, 1510, 1232, 1074 cm^{-1} .

Example 52Ethyl 4-(2-chloro-5-methoxyphenyl)-4,7-dihydro-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-5-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

5 MP:182°C.

Anal. Calcd. for: C₁₉H₂₂ClN₃O₃: C, 60.72; H, 5.90; N, 11.18.

Found: C, 60.58; H, 5.88; N, 11.07.

MS(EI): 375 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H, t, J=7.3Hz),

10 0.99(3H, t, J=7.3Hz), 1.64-1.69(2H, m), 2.64-2.67(1H, m), 2.87-

2.90(1H, m), 3.79(2H, q, J=7.3Hz), 3.86(3H, s), 5.44(1H, s),

6.85(1H, d, J=7.3Hz), 6.94(1H, d, J=7.3Hz), 7.10(1H, dd, J=2.9Hz and

7.3Hz), 7.17(1H, s), 9.43(1H, br.s), 11.91(1H, br.s).

Example 53

15 Ethyl 4-(2,5-dimethoxyphenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,5-dimethoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

20 MP:169-170°C.

MS(EI): 371 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H, t, J=7.3Hz),

0.98(3H, t, J=7.3Hz), 1.68-1.70(2H, m), 2.49-2.54(1H, m), 2.94-

2.97(1H, m), 3.57(3H, s), 3.79-3.83(2H, m), 3.80(3H, s),

25 4.02(1H, q, J=7.3Hz), 5.43(1H, s), 6.49(1H, d, J=2.9Hz),

6.59(1H, dd, J=2.9Hz and 8.8Hz), 6.82(1H, d, J=8.8Hz), 7.14(1H, s),

9.32(1H, br.s), 11.83(1H, br.s).

Example 54

30 Ethyl 4-(2,6-difluorophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,6-difluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:185°C.

Anal. Calcd. for: $C_{18}H_{19}F_2N_3O_2 \cdot 1/2 H_2O$: C, 60.67; H, 5.66; N, 11.79.

Found: C, 60.68; H, 5.46; N, 11.61.

MS(EI): 347 (M^+).

- 5 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90-0.97(6H, m), 1.54-1.58(2H, m), 2.51-2.54(1H, m), 2.76-2.81(1H, m), 3.82(2H, q, $J=7.3$ Hz), 5.53(1H, s), 6.90(2H, dd, $J=7.3$ Hz and 7.3Hz), 7.16(1H, d, $J=7.3$ Hz), 7.20(1H, s), 9.50(1H, br.s), 11.96(1H, br.s).

Example 55

- 10 Ethyl 4-(2,6-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,6-dichlorobenzaldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

- 15 MP:202°C.

Anal. Calcd. for: $C_{18}H_{19}Cl_2N_3O_2 \cdot 3/10 H_2O$: C, 56.06; H, 5.12; N, 10.90.

Found: C, 56.28; H, 5.46; N, 10.78.

MS(EI): 380 (M^+).

- 20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.83(3H, t, $J=7.3$ Hz), 0.92(3H, t, $J=7.3$ Hz), 1.57-1.62(2H, m), 2.47-2.51(1H, m), 2.77-2.80(1H, m), 3.74(2H, q, $J=7.3$ Hz), 6.03(1H, s), 7.05(1H, s), 7.13(1H, dd, $J=7.3$ Hz and 7.4Hz), 7.22(1H, d, $J=7.3$ Hz), 7.39(1H, d, $J=7.3$ Hz), 9.53(1H, br.s), 11.93(1H, br.s).

Example 56

- 25 Ethyl 4-(2-chloro-6-fluorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chloro-6-fluorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

- 30 MP:180-183°C.

MS(EI): 363 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, $J=6.9$ Hz), 0.94(3H, t, $J=7.3$ Hz), 1.56-1.61(2H, m), 2.50-2.85(2H, m),

3.80(2H,q,J=7.3Hz), 5.75(1H,s), 7.01-7.17(4H,m), 9.52(1H,br.s),
11.97(1H,br.s).

IR(KBr): ν =3265,1591,1518,1456,1228,1097 cm^{-1} .

Example 57

5 Ethyl 4,7-dihydro-6-propyl-4-(pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate dihydrochloride

The title compound was prepared from pyridine-3-aldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:251°C.

10 Anal. Calcd. for: $\text{C}_{17}\text{H}_{20}\text{N}_4\text{O}_2 \cdot 2\text{HCl}$:C,52.99;H,5.76;N,14.54.

Found:C,52.99;H,5.67;N,14.44.

MS(EI):312(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.91(3H,t,J=7.3Hz),

1.09(3H,t,J=7.3Hz), 1.52-1.61(2H,m), 2.66-2.71(2H,m), 3.93-

15 4.00(2H,m), 5.24(1H,s), 7.90(1H,dd,J=7.3Hz and 7.4Hz), 8.31-

8.35(2H,m), 8.66-8.69(2H,m), 10.35(1H,br.s).

Example 58

Ethyl 4,7-dihydro-6-propyl-4-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate dihydrochloride

20 The title compound was prepared from pyridine-4-aldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:266°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{20}\text{N}_4\text{O}_2 \cdot 2\text{HCl}$:C,52.99;H,5.76;N,14.54.

Found:C,52.63;H,5.65;N,14.69.

25 MS(EI):312(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.91(3H,t,J=7.3Hz),

1.12(3H,t,J=7.3Hz), 1.52-1.59(2H,m), 2.64-2.72(2H,m),

4.01(2H,q,J=7.3Hz), 5.30(1H,s), 7.76(2H,d,J=6.4Hz), 8.66(1H,s),

8.72(2H,d,J=6.4Hz), 10.39(1H,br.s).

30 **Example 59**

Ethyl 4-(furan-2-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from furan-2-aldehyde,

3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:108-111°C.

MS(EI):301(M⁺).

5 ¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.92(3H,t,J=7.3Hz),
1.05(3H,t,J=6.8Hz), 1.58(2H,q,J=7.3Hz), 2.66-2.72(2H,m),
3.50(3H,br.s), 3.94(2H,q,J=6.8Hz),5.21(1H,s),5.78(1H,d,
J=2.9Hz),6.23(1H,s), 6.24(2H,s), 7.75(1H,s), 7.38(1H,s),
9.42(1H,br.s).

10 IR(KBr):ν=3207,2962,1703,1479,1348,1205,1076,866cm⁻¹.

Example 60

Ethyl 4-(furan-3-yl)-4,7-dihydro-4-(furan-3-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from furan-3-aldehyde,
15 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:121-123°C.

Anal. Calcd. for:C₁₆H₁₉N₃O₃C₄H₄O₄:C,57.54;H,5.55;N,10.07.

Found:C,57.14;H,5.55;N,10.37.

20 MS(EI):301(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.90(3H,t,J=7.3Hz),
1.08(3H,t,J=7.4Hz), 1.55-1.57(2H,m), 2.62-2.70(2H,m),
3.36(1H,br.s), 3.50(2H,br.s), 3.97(2H,q,J=7.3Hz), 5.06(1H,s),
6.16(1H,s), 6.24(2H,s), 7.13(1H,s), 7.35(1H,s), 7.40(1H,s),
25 9.31(1H,br.s).

IR(KBr):ν=3350,2972,1591,1467,1361,1203,1089cm⁻¹.

Example 61

Ethyl 4,7-dihydro-4-(2-methylfuran-3-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 2-methylfuran-3-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:123-125°C.

Anal. Calcd. for: $C_{17}H_{21}N_3O_3$ 2/5 H_2O : C, 63.30; H, 6.81; N, 13.03.

Found: C, 63.51; H, 6.64; N, 12.96.

MS(EI): 315 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.93(3H, t, J=7.3Hz),
5 1.08(3H, t, J=7.3Hz), 1.58-1.60(2H, m), 2.20(3H, s), 2.55-
2.75(2H, m), 3.92(2H, q, J=7.3Hz), 4.99(1H, s), 5.96(1H, s),
7.21(2H, s), 9.26(1H, br.s), 11.91(1H, br.s).

IR(KBr): ν =3265, 3198, 2964, 1591, 1514, 1224, 1209, 1093 cm^{-1} .

Example 62

10 Ethyl 4,7-dihydro-6-propyl-4-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from thiophene-2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

15 MP: 129-131°C.

Anal. Calcd. for: $C_{16}H_{19}N_3O_2SC_4H_4O_4$ 1/4 H_2O : C, 54.85; H, 5.41; N, 9.59.

Found: C, 54.59; H, 5.22; N, 9.97.

MS(EI): 317 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, J=7.4Hz),
20 1.06(3H, t, J=7.3Hz), 1.58-1.60(2H, m), 2.72-2.74(2H, m),
3.50(3H, br.s), 3.94(2H, q, J=7.4Hz), 5.44(1H, s), 6.25(2H, s),
6.69(1H, s), 6.81(1H, d), 7.15(1H, d), 7.37(1H, s), 9.50(1H, br.s).

Example 63

25 Ethyl 4,7-dihydro-4-(3-methylthiophen-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3-methylthiophene-2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 125°C.

30 Anal. Calcd. for: $C_{17}H_{21}N_3O_2S$ H_2O : C, 58.43; H, 6.63; N, 12.02.

Found: C, 58.59; H, 6.33; N, 12.12.

MS(EI): 331 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.96(3H, t, J=7.4Hz),

0.98(3H,t,J=7.3Hz), 1.60-1.63(2H,m), 2.22(3H,s), 2.83-
2.90(2H,m), 3.88(2H,q,J=7.3Hz), 5.42(1H,s), 6.68(1H,d,J=4.9Hz),
7.02(1H,d,J=5.4Hz), 7.29(1H,s), 9.45(1H,br.s), 11.98(1H,br.s).
IR(KBr): ν =3267,3196,2968,1664,1510,1267,1201,1091 cm^{-1} .

5 **Example 64**

Ethyl 4-(5-chlorothiophen-2-yl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 5-chlorothiophene-
2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the
10 same manner as in Example 25.

MP:129-131°C.

Anal. Calcd. for: $\text{C}_{16}\text{H}_{18}\text{N}_3\text{O}_2\text{SC}_4\text{H}_4\text{O}_4$: C, 51.33; H, 4.74; N, 8.98.

Found: C, 51.34; H, 4.54; N, 9.03.

MS(EI): 351(M^+).

15 ^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H,t,J=7.3Hz),
1.10(3H,t,J=6.9Hz), 1.59-1.61(2H,m), 2.57-2.82(2H,m),
3.50(2H,br.s), 3.38(1H,s), 3.98(2H,q,J=6.9Hz), 5.36(1H,s),
6.25(2H,s), 6.53(1H,d,J=3.9Hz), 6.80(1H,d,J=3.4Hz), 7.42(1H,s),
9.60(1H,br.s).

20 IR(KBr): ν =3205,2964,2629,1618,1471,1363,1205,1080,889,652 cm^{-1} .

Example 65

Ethyl 4,7-dihydro-6-propyl-4-(thiophen-3-yl)-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate maleate

The title compound was prepared from thiophene-3-
25 aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the
same manner as in Example 25.

MP:141-143°C.

Anal. Calcd. for: $\text{C}_{16}\text{H}_{19}\text{N}_3\text{O}_2\text{SC}_4\text{H}_4\text{O}_4$: C, 54.42; H, 5.35; N, 9.69.

Found: C, 54.17; H, 5.23; N, 9.66.

30 MS(EI): 317(M^+).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H,t,J=7.3Hz),
1.03(3H,t,J=6.8Hz), 1.59-1.61(2H,m), 2.60-2.78(2H,m),
3.50(2H,br.s), 3.91(2H,q,J=6.8Hz), 5.22(2H,s), 6.26(2H,s),

6.84-6.88(2H,m), 7.29(1H,dd,J=3.0Hz and 4.9Hz), 7.33(1H,s),
12.0(1H,br.s).

IR(KBr): ν =3346,2980,2611,1697,1467,1361,1205,1087 cm^{-1} .

Example 66

5 Ethyl 4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from naphthalene-1-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

10 MP:182°C.

Anal. Calcd. for: $\text{C}_{22}\text{H}_{23}\text{N}_3\text{O}_2$:C,73.11;H,6.41;N,11.63.

Found:C,72.95;H,6.47;N,11.40.

MS(EI):361(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.62(3H,t,J=7.3Hz),
15 1.00(3H,t,J=7.3Hz), 1.69-1.73(2H,m), 2.73-2.76(1H,m), 2.84-
2.87(1H,m), 3.67(2H,q,J=7.3Hz), 5.95(1H,s), 7.03(1H,s),
7.23(1H,d,J=7.3Hz), 7.36(1H,dd,J=7.3Hz and 7.4Hz),
7.49(1H,dd,J=7.3Hz and 7.4Hz), 7.57(1H,dd,J=7.3Hz and 7.4Hz),
7.65(1H,d,J=7.3Hz), 7.88(1H,d,J=7.3Hz), 8.40(1H,d,J=7.3Hz),
20 9.45(1H,br.s), 11.82(1H,br.s).

Example 67

Ethyl 4,7-dihydro-4-(naphthalen-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from naphthalene-2-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the
25 same manner as in Example 25.

MP:136-138°C.

Anal. Calcd. for: $\text{C}_{22}\text{H}_{23}\text{N}_3\text{O}_2\cdot\text{C}_4\text{H}_4\text{O}_4 \cdot 1/4 \text{H}_2\text{O}$:C,64.79;H,5.75;N,8.72.

Found:C,64.86;H,5.57;N,8.99.

30 MS(EI):361(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.92-0.98(6H,m), 1.64-1.68(2H,m),
2.72-2.80(2H,m), 3.50(2H,br.s), 3.80(2H,q,J=7.3Hz), 5.27(1H,s),
6.25(2H,s),7.23(1H,s), 7.31(1H,d,J=8.3Hz), 7.41-7.43(2H,m),

7.57(1H,s), 7.73-7.77(2H,m), 9.47(1H,br.s).

IR(KBr): ν =3202,2962,1701,1464,1359,1222 cm^{-1} .

Example 68

Ethyl 4,7-dihydro-4-(2-methoxynaphthalen-1-yl)-6-propyl-2H-
5 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxynaphthalene-1-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:188-191°C.

10 Anal. Calcd. for: $\text{C}_{23}\text{H}_{25}\text{N}_3\text{O}_3 \cdot 2/5 \text{H}_2\text{O}$: C, 69.29; H, 6.52; N, 10.54.

Found: C, 69.35; H, 6.62; N, 10.21.

MS(EI): 391(M^+).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.71(3H,t, $J=7.3\text{Hz}$),

0.95(3H,t, $J=7.3\text{Hz}$), 1.62-1.63(2H,m), 2.49-2.86(2H,m),

15 3.61(2H,q, $J=7.3\text{Hz}$), 3.97(3H,s), 6.27(1H,s), 6.89(1H,s), 7.16-

7.51(3H,m), 7.71-7.77(2H,m), 7.98(1H,s), 9.43(1H,br.s),

11.77(1H,br.s).

IR(KBr): ν =3258,1655,1593,1082 cm^{-1} .

Example 69

20 Ethyl 4-(2,3-dihydrobenzo[b]furan-7-yl)-4,7-dihydro-6-propyl-
2H- pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-dihydrobenzo[b]furan-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

25 MP:194-196°C.

Anal. Calcd. for: $\text{C}_{20}\text{H}_{23}\text{N}_3\text{O}_3$: C, 67.97; H, 6.56; N, 11.89.

Found: C, 67.97; H, 6.68; N, 11.77.

MS(EI): 353(M^+).

^1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H,t, $J=7.4\text{Hz}$),

30 0.97(3H,t, $J=7.3\text{Hz}$), 1.66(2H,m), 2.67-2.70(1H,m), 2.82-

2.84(1H,m), 3.15(2H,t, $J=8.8\text{Hz}$), 3.83-3.86(2H,m), 4.55-

4.58(2H,m), 5.29(1H,s), 6.64(1H,dd, $J=7.3\text{Hz}$ and 7.4Hz),

6.72(1H,d, $J=6.9\text{Hz}$), 6.93(1H,dd, $J=7.3\text{Hz}$ and 7.4Hz), 7.20(1H,s),

9.32(1H,br.s), 11.86(1H,br.s).

Example 70

Ethyl 4-(5-bromo-2,3-dihydrobenzo[b]furan-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 The title compound was prepared from 5-bromo-2,3-dihydrobenzo[b]furan-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:200-210°C.

Anal. Calcd. for: C₂₀H₂₂BrN₃O₃: C, 55.57; H, 5.13; N, 9.72.

10 Found: C, 55.23; H, 5.09; N, 9.89.

MS(EI): 432(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.93-0.98(6H,m),

1.64(2H,q,J=7.3Hz), 2.63(1H,m), 2.88-2.90(1H,m),

3.16(2H,t,J=8.3Hz), 3.85-3.87(2H,m), 4.57-4.60(2H,m),

15 5.23(1H,s), 6.78(1H,s), 7.11(1H,s), 7.22(1H,s), 9.44(1H,br.s),

11.94(1H,br.s).

Example 71

Ethyl 4-(5-chloro-2,3-dihydro-2-methylbenzo[b]furan-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 maleate

The title compound was prepared from 5-chloro-2,3-dihydro-2-methylbenzo[b]furan-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:155-158°C.

25 Anal. Calcd. for: C₂₁H₂₄N₃O₃C₄H₄O₄: C, 57.95; H, 5.45; N, 8.11.

Found: C, 57.57; H, 5.28; N, 8.47.

MS(EI): 401(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(6H,t,J=6.8Hz),

1.03(3H,d,J=6.3Hz), 1.65(2H,m), 2.40-2.73(2H,m), 2.87(1H,m),

30 3.29(1H,m), 3.50(3H,br.s), 3.84(2H,q,J=6.8Hz), 5.05(1H,m),

5.23(1H,s), 6.25(2H,s), 6.64(1H,s), 6.95(1H,s),

7.20(1H,d,J=4.4Hz), 9.43(1H,br.s).

IR(KBr): ν=3207, 2976, 1589, 1462, 1201, 1082cm⁻¹.

Example 72

Ethyl 4-(2H-1-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2H-1-benzopyran-8-
5 aldehyde and ethyl 3-ketohexanoate in the same manner as in
Example 39.

MP:194°C.

Anal. Calcd. for: $C_{21}H_{23}N_3O_3$: C, 69.02; H, 6.34; N, 11.50.

Found: C, 68.60; H, 6.43; N, 11.25.

10 MS(EI): 194 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.90(3H, t, J=7.3Hz),
0.96(3H, t, J=7.3Hz), 1.64-1.68(2H, m), 2.62-2.66(1H, m), 2.80-
2.84(1H, m), 3.81(2H, q, J=7.3Hz), 4.85(2H, dd, J=2.0Hz and 9.8Hz),
5.39(1H, s), 5.89(1H, d, J=9.8Hz), 6.46(1H, d, J=9.8Hz), 6.67-
15 6.80(3H, m), 7.18(1H, s), 9.31(1H, br.s), 11.86(1H, br.s).

Example 73

Ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 3,4-dihydro-2H-
20 benzopyran-8-aldehyde and ethyl 3-ketohexanoate in the same
manner as in Example 39.

MP:208°C.

Anal. Calcd. for: $C_{21}H_{25}N_3O_3 \cdot 1/2 H_2O$: C, 67.01; H, 6.96; N, 11.16.

Found: C, 67.41; H, 6.84; N, 10.93.

25 MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.63-1.68(2H, m), 1.92-1.96(2H, m), 2.67-
2.82(4H, m), 3.80(2H, q, J=7.3Hz), 4.22-4.26(2H, m), 5.41(1H, s),
6.61(1H, dd, J=7.3Hz and 7.4Hz), 6.71-6.75(2H, m), 7.17(1H, s),
30 9.25(1H, br.s), 11.80(1H, br.s).

Example 74

Ethyl 4,7-dihydro-6-propyl-4-(quinolin-4-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from quinoline-4-aldehyde and ethyl 3-ketohexanoate in the same manner as in Example 39.

MP:198°C.

5 Anal. Calcd. for: $C_{21}H_{22}N_4O_2 \cdot 2/5 H_2O$: C, 68.24; H, 6.22; N, 15.16.

Found: C, 68.39; H, 6.04; N, 14.83.

MS(EI): 362 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.61(3H, t, J=7.3Hz),
1.02(3H, t, J=7.3Hz), 1.68-1.72(2H, m), 2.76-2.78(1H, m), 2.86-
10 2.89(1H, m), 3.66-3.68(2H, m), 5.97(1H, s), 7.07(1H, s),
7.17(1H, d, J=4.4Hz), 7.65(1H, dd, J=7.3Hz and 7.4Hz),
7.74(1H, dd, J=7.3Hz and 7.4Hz), 7.99(1H, d, J=7.3Hz),
8.48(1H, d, J=7.8Hz), 8.73(1H, d, J=4.4Hz), 9.61(1H, br.s),
11.94(1H, br.s).

15 **Example 75**

Ethyl 4-(benzo[b]thiophen-3-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from benzo[b]thiophene-3-aldehyde and ethyl 3-ketohexanoate in the same manner as in
20 Example 39.

MP:222°C.

Anal. Calcd. for: $C_{20}H_{21}N_3O_2S$: C, 65.37; H, 5.76; N, 11.44.

Found: C, 65.11; H, 5.31; N, 11.83.

MS(EI): 238 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.64(3H, t, J=7.3Hz),
1.20(3H, t, J=7.3Hz), 1.56-1.58(2H, m), 2.66-2.78(2H, m),
4.11(2H, q, J=7.3Hz), 4.89(1H, s), 7.42-7.50(2H, m), 7.55(1H, s),
7.61(1H, s), 7.96-8.01(2H, m), 10.32(1H, br.s), 12.13(1H, br.s).

Example 76

30 Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-

ketohehexanoate in the same manner as in Example 39.

MP:207°C.

Anal. Calcd. for: C₁₈H₁₉N₅O₃: C, 61.18; H, 5.42; N, 19.82.

Found: C, 61.06; H, 5.50; N, 19.66.

5 MS(EI): 353(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.77(3H, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 2.72-2.77(1H, m), 2.82-2.86(1H, m),
3.79(2H, q, J=7.3Hz), 5.68(1H, s), 7.11(1H, d, J=7.3Hz), 7.22(1H, s),
7.51(1H, dd, J=7.3Hz and 7.4Hz), 7.78(1H, d, J=7.3Hz),

10 9.66(1H, br.s), 12.01(1H, br.s).

Example 77

Ethyl 4-(1,3-benzdioxazol-4-yl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 1,3-benzdioxazole-
15 4-aldehyde, 3-aminopyrazole and ethyl 3-ketohehexanoate in the
same manner as in Example 25.

MP:203-207°C.

Anal. Calcd. for: C₁₉H₂₁N₃O₄ 1/10 H₂O: C, 63.89; H, 5.98; N, 11.76.

Found: C, 63.72; H, 5.86; N, 12.01.

20 MS(EI): 355(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz),
0.96(3H, t, J=7.4Hz), 1.61-1.67(2H, m), 2.64-2.82(2H, m), 3.80-
3.88(2H, m), 5.28(1H, s), 5.99(1H, s), 6.00(1H, d, J=9.7Hz),
6.50(1H, d, J=5.9Hz), 6.65(1H, s), 6.65-6.69(1H, m), 7.25(1H, s),

25 9.40(1H, br.s), 11.94(1H, br.s).

IR(KBr): ν=3265, 3188, 2962, 1662, 1587, 1514, 1462, 1253, 1215, 1066cm⁻¹.

Example 78

Ethyl 4-(6-chloro-3,4-dihydro-2,2-dimethyl-2H-1,4-benzoxazin-
8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-
30 carboxylate maleate

The title compound was prepared from 6-chloro-3,4-
dihydro-2,2-dimethyl-2H-1,4-benzoxazine-8-aldehyde, 3-
aminopyrazole and ethyl 3-ketohehexanoate in the same manner as

in Example 25.

MS(EI):430(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.92(3H,t,J=7.4Hz),
0.96(3H,t,J=7.3Hz), 1.18(3H,s), 1.32(3H,s), 1.62-1.64(2H,m),
5 2.66-2.82(2H,m), 2.99(2H,s), 3.80(2H,t,J=7.3Hz), 5.32(1H,s),
6.01(2H,s), 6.14(1H,s), 6.32(1H,s), 7.14(1H,s), 9.31(1H,br.s),
11.82(1H,br.s).

IR(KBr):ν=3281,2974,1672,1599,1520,1207,1155,1091cm⁻¹.

Example 79

10 Ethyl 4-(6-chloro-3,4-dihydro-2,2,4-trimethyl-1,4-benzoxazin-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 6-chloro-3,4-dihydro-2,2,4-trimethyl-2H-1,4-benzoxazine-8-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as
15 in Example 25.

MS(EI):444(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.91(3H,t,J=7.3Hz),
0.96(3H,t,J=7.3Hz), 1.20(6H,s), 1.35(3H,s), 1.63-1.65(2H,m),
20 2.83(2H,s), 3.00(2H,q,J=7.3Hz), 5.34(1H,s), 6.26(2H,s),
6.43(1H,d,J=2.5Hz), 7.13(1H,s), 9.33(1H,s), 11.82(1H,br.s).

IR(KBr):ν=3273,2974,1666,1597,1518,1458,1259,1211cm⁻¹.

Example 80

25 Ethyl 4-(2,3-dihydro-1,4-benzodioxin-6-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from 2,3-dihydro-1,4-benzodioxin-6-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:147-149°C.

30 Anal. Calcd. for:C₂₀H₂₃N₃O₄C₄H₄O₄:C,59.37;H,5.60;N,8.66.

Found:C,59.12;H,5.63;N,8.57.

MS(EI):369(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.93(3H,t,J=7.3Hz),

1.02(3H,t,J=6.8Hz), 1.60(2H,q,J=7.3Hz), 2.64-2.68(2H,m),
3.50(2H,br.s), 3.86(2H,q,J=7.3Hz), 4.14(4H,s), 4.99(1H,s),
6.26(2H,s), 6.54(1H,s), 6.57(1H,d,J=7.8Hz), 6.65(1H,d,J=7.8Hz),
7.21(1H,s), 11.97(1H,br.s).

5 IR(KBr): ν =3211,2694,2878,2658,1697,1506,1466,1363,1302,1082 cm^{-1} .

Example 81

Ethyl 4-(benzo[b]furan-2-yl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate maleate

The title compound was prepared from benzo[b]furan-2-
10 aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the
same manner as in Example 25.

MP:123-125°C.

Anal. Calcd. for: $\text{C}_{20}\text{H}_{21}\text{N}_3\text{O}_3\text{C}_4\text{H}_4\text{O}_4 \cdot 1/2 \text{H}_2\text{O}$:C,61.19;H,5.43;N,8.92.

Found:C,61.02;H,5.41;N,9.27.

15 MS(EI):351(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.96(3H,t,J=7.3Hz),
1.02(3H,t,J=6.8Hz), 1.63(2H,q,J=7.3Hz), 2.73-2.76(2H,m),
3.50(3H,br.s), 3.93(2H,q,J=7.3Hz), 5.36(1H,s), 6.24(2H,s),
6.43(1H,s), 7.10-7.21(2H,m), 7.41-7.48(3H,m), 9.51(1H,br.s).

20 IR(KBr): ν =3190,3080,2962,1705,1581,1454,1359,1195,883 cm^{-1} .

Example 82

Ethyl 4-(2-chlorophenyl)-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

The title compound was prepared from 2-
25 chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketopentanoate
in the same manner as in Example 1.

MP:213°C.

Anal. Calcd. for: $\text{C}_{17}\text{H}_{18}\text{ClN}_3\text{O}_2$:C,61.54;H,5.47;N,12.66.

Found:C,61.54;H,5.46;N,12.68.

30 MS(EI):331(M^+).

^1H -NMR (400MHz,DMSO- d_6) δ (ppm): 0.85(3H,t,J=7.3Hz),
1.21(3H,t,J=7.3Hz), 2.78-2.84(2H,m), 3.78(2H,q,J=7.3Hz),
5.58(1H,s), 7.07-7.12(2H,m), 7.18(1H,dd,J=7.3Hz and

7.4Hz), 7.25(1H,s), 7.34(1H,d,J=7.3Hz), 9.52(1H,br.s),
11.97(1H,br.s).

Example 83

Ethyl 6-butyl-4-(2-chlorophenyl)-4,7-dihydro-2H-pyrazolo[3,4-
5 b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 1.

MP:209°C.

10 Anal. Calcd. for: C₁₉H₂₂ClN₃O₂ 1/5 H₂O: C, 62.79; H, 6.21; N, 11.56.

Found: C, 62.78; H, 6.11; N, 11.45.

MS(EI): 359(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H,t,J=7.3Hz),
0.92(3H,t,J=7.3Hz), 1.36-1.42(2H,m), 1.60-1.64(2H,m), 2.72-
15 2.76(1H,m), 2.83-2.86(1H,m), 3.78(2H,q,J=7.3Hz), 5.58(1H,s),
7.07-7.11(2H,m), 7.18(1H,dd,J=7.3Hz and 7.4Hz), 7.24(1H,s),
7.34(1H,d,J=7.3Hz), 9.49(1H,br.s), 11.96(1H,br.s).

Example 84

Methyl 4-(2-chlorophenyl)-4,7-dihydro-6-methoxymethyl-2H-
20 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and methyl 4-methoxyacetoacetate in the same manner as in Example 1.

MP:160°C.

25 Anal. Calcd. for: C₁₆H₁₆ClN₃O₃: C, 57.33; H, 4.83; N, 12.59.

Found: C, 57.53; H, 4.86; N, 12.58.

MS(EI): 333(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.36(3H,s), 3.38(3H,s),
4.67(2H,s), 5.58(1H,s), 7.08-7.13(2H,m), 7.19(1H,dd,J=7.3Hz
30 and 7.4Hz), 7.32-7.36(2H,m), 9.14(1H,br.s), 12.08(1H,br.s).

Example 85

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl benzoylacetoacetate in the same manner as in Example 1.

MP:214°C.

5 Anal. Calcd. for: $C_{21}H_{18}ClN_3O_2 \cdot 3/10 H_2O$: C, 65.47; H, 4.87; N, 10.91.

Found: C, 65.29; H, 4.73; N, 10.93.

MS(EI): 379 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.57(3H, t, J=7.3Hz),
3.52(2H, q, J=7.3Hz), 5.65(1H, s), 7.14(1H, dd, J=7.3Hz and 7.4Hz),
10 7.27(1H, dd, J=7.3Hz and 7.4Hz), 7.37-7.40(8H, m), 9.53(1H, br.s),
12.04(1H, br.s).

Example 86

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl (4-methoxybenzoyl)acetate in the same manner as in Example 1.

MP:211°C.

Anal. Calcd. for: $C_{22}H_{20}ClN_3O_3$: C, 64.47; H, 4.92; N, 10.25.

20 Found: C, 64.30; H, 5.00; N, 10.24.

MS(EI): 409 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.64(3H, t, J=7.3Hz),
3.56(2H, q, J=7.3Hz), 3.79(3H, s), 5.63(1H, s), 6.95(2H, d, J=7.3Hz),
7.13(1H, dd, J=7.3Hz and 7.4Hz), 7.24-7.38(6H, m), 9.45(1H, br.s),
25 12.03(1H, br.s).

Example 87

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl (thiophen-2-carbonyl)acetate in the same manner as in Example 1.

MP:200°C.

Anal. Calcd. for: $C_{19}H_{16}ClN_3O_2S$: C, 59.14; H, 4.18; N, 10.89.

Found: C, 59.04; H, 4.31; N, 11.14.

MS(EI): 385(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.02(3H, t, J=7.3Hz),
4.04(2H, q, J=7.3Hz), 5.16(1H, s), 6.58(1H, d, J=7.3Hz), 7.18-
5 7.70(7H, m), 9.60(1H, br.s), 12.74(1H, br.s).

Example 88

Ethyl 6-benzyl-4-(2-chlorophenyl)-4,7-dihydro-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

The title compound was prepared from 2-
10 chlorobenzaldehyde, 3-aminopyrazole and ethyl 4-
phenylacetoacetate in the same manner as in Example 1.

MP: 247°C.

Anal. Calcd. for: C₂₂H₂₀ClN₃O₂ 1/5 H₂O: C, 66.48; H, 5.17; N, 10.57.

Found: C, 66.30; H, 5.17; N, 10.37.

15 MS(EI): 393(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.81(3H, t, J=7.3Hz),
3.76(2H, q, J=7.3Hz), 4.25(2H, s), 5.65(1H, s), 7.06-7.41(10H, m),
9.68(1H, br.s), 12.01(1H, br.s).

Example 89

20 Ethyl 6-ethyl-4,7-dihydro-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-
b]pyridine-5-carboxylate

The title compound was prepared from 2-
methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-
ketopentanoate in the same manner as in Example 1.

25 MP: 169°C.

Anal. Calcd. for: C₁₈H₂₁N₃O₃ 3/10 H₂O: C, 64.97; H, 6.54; N, 12.63.

Found: C, 64.86; H, 6.84; N, 12.33.

MS(EI): 327(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=7.3Hz),
30 1.18(3H, t, J=7.3Hz), 2.73-2.76(1H, m), 2.81-2.85(1H, m),
3.74(2H, q, J=7.3Hz), 3.85(3H, s), 5.46(1H, s), 6.76(1H, dd, J=7.3Hz
and 7.4Hz), 6.89-6.94(2H, m), 7.04(1H, dd, J=7.3Hz and 7.4Hz),
7.14(1H, s), 9.32(1H, br.s), 11.82(1H, br.s).

Example 90Ethyl 6-butyl-4,7-dihydro-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 1.

MP:190°C.

Anal. Calcd. for: $C_{20}H_{25}N_3O_3 \cdot 1/2 H_2O$: C, 65.91; H, 7.19; N, 11.53.

Found: C, 65.92; H, 7.07; N, 11.88.

MS(EI): 355 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.85(3H, t, J=7.3Hz), 0.93(3H, t, J=7.3Hz), 1.38-1.44(2H, m), 1.59-1.64(2H, m), 2.64-2.68(1H, m), 2.85-2.90(1H, m), 3.81(2H, q, J=7.3Hz), 3.85(3H, s), 5.47(1H, s), 6.76(1H, dd, J=7.3Hz and 7.4Hz), 6.89-6.94(2H, m), 7.04(1H, dd, J=7.3Hz and 7.4Hz), 7.14(1H, s), 9.29(1H, br.s), 11.82(1H, br.s).

Example 91Methyl 4,7-dihydro-6-methoxymethyl-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and methyl 4-methoxyacetoacetate in the same manner as in Example 1.

MP:186°C.

Anal. Calcd. for: $C_{17}H_{19}N_3O_4 \cdot 1/5 H_2O$: C, 61.32; H, 5.87; N, 12.62.

Found: C, 61.34; H, 5.84; N, 12.52.

MS(EI): 329 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.36(3H, s), 3.38(3H, s), 3.86(3H, s), 4.68(2H, s), 5.46(1H, s), 6.77(1H, dd, J=7.3Hz and 7.4Hz), 6.90-6.94(2H, m), 7.06(1H, dd, J=7.3Hz and 7.4Hz), 7.22(1H, s), 8.94(1H, br.s), 11.94(1H, br.s).

Example 92Ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxybenzaldehyde, 3-aminopyrazole and ethyl benzoylacetate in the same manner as in Example 1.

MP: 195°C.

5 Anal. Calcd. for: C₂₂H₂₁N₃O₃: C, 70.38; H, 5.64; N, 11.19.

Found: C, 70.41; H, 5.71; N, 11.27.

MS(EI): 375(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.55(3H, t, J=7.3Hz),
3.53(2H, q, J=7.3Hz), 3.88(3H, s), 5.52(1H, s), 6.84(1H, dd, J=7.3Hz
10 and 7.4Hz), 6.94(1H, d, J=7.3Hz), 7.09(1H, dd, J=7.3Hz and 7.4Hz),
7.18(1H, d, J=7.3Hz), 7.23(1H, s), 7.37-7.40(5H, m), 9.33(1H, br.s),
11.90(1H, br.s).

Example 93

4-(2-Chlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-
15 pyrazolo[3,4-b]pyridine

To an aqueous solution (50 mL) of nitromethane (50 g) was added an aqueous solution (50 mL) of n-butylaldehyde (59 g), and the mixture was stirred with heating at 60°C for 6 hours. The reaction mixture was allowed to cool to ambient
20 temperature, and extracted with ethyl acetate. The solvent was evaporated under reduced pressure to give a brown oil (58 g). To a mixed solution of the obtained oil (50 g) in water (50 mL) and acetone (50 mL) was added sodium chromate (70 g). Under ice-cooling, concentrated sulfuric acid (46 mL) was
25 added dropwise and the mixture was stirred for 5 hours. Ice-water (200 mL) was added and the mixture was extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give
30 1-nitropentan-2-one (40 g) as a brown oil. A solution of 2-chlorobenzaldehyde (1.8 g), 3-aminopyrazole (1.0 g) and 1-nitropentan-2-one (1.4 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to

room temperature, and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (680 mg) as yellow crystals.

5 MP:228°C.

Anal. Calcd. for: $C_{15}H_{15}ClN_4O_2$: C, 56.52; H, 4.74; N, 17.58.

Found: C, 56.26; H, 4.91; N, 17.64.

MS(EI): 318 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.02(3H, t, J=7.3Hz), 1.70-
10 1.73(2H, m), 2.89-2.91(1H, m), 2.99-3.02(1H, m), 5.90(1H, s),
7.09-7.21(3H, m), 7.39(1H, d, J=7.3Hz), 7.44(1H, s),
10.84(1H, br.s), 12.43(1H, br.s).

Example 94

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-
15 pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (4.8 g) in THF (150 mL) was added n-BuLi (67 mmol) at -78°C. Further, methyl butanoate (10 g) was added and the mixture was stirred for one hour. After acidification with hydrochloric acid, the mixture was
20 extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give 1-cyanopentan-2-one (5.5 g) as a colorless oil. A solution of 2-chlorobenzaldehyde (1.9 g), 3-aminopyrazole (1.0
25 g) and 1-cyanopentan-2-one (1.6 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated crystals were collected by filtration to give the title compound (1.3 g) as colorless crystals.

30 MP:248°C.

Anal. Calcd. for: $C_{16}H_{15}ClN_4$: C, 64.32; H, 5.06; N, 18.75.

Found: C, 64.49; H, 5.18; N, 18.81.

MS(EI): 298 (M^+).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.95(3H, t, J=7.3Hz), 1.64-1.70(2H, m), 2.38-2.42(2H, m), 5.36(1H, s), 7.23-7.26(3H, m), 7.32(1H, dd, J=7.3Hz and 7.4Hz), 7.42(1H, d, J=7.3Hz), 9.83(1H, br.s), 12.15(1H, br.s).

5 **Example 95**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (76 g) in DMSO (100 mL) was added methyl p-anisate (100 g) and the mixture was stirred with heating at 60°C for one hour. The reaction mixture was allowed to cool, and cold water (500 mL) was added dropwise. The mixture was acidified with hydrochloric acid and the precipitated crystals were collected by filtration. The obtained crystals were extracted with ethyl acetate and the solvent was evaporated under reduced pressure. The residue was recrystallized from ethyl acetate to give benzoylacetonitrile (60 g) as colorless crystals. A solution of 2-chlorobenzaldehyde (1.7 g), 3-aminopyrazole (1.0 g) and benzoylacetonitrile (1.8 g) in acetonitrile (20 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the precipitated crystals were collected by filtration to give the title compound (2.63 g) as colorless crystals.

MP:124°C.

25 Anal. Calcd. for: C₂₀H₁₅ClN₄O 8/5 H₂O: C, 61.34; H, 4.68; N, 14.31.

Found: C, 61.32; H, 4.88; N, 14.31.

MS(EI): 362(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.81(3H, s), 5.48(1H, s), 7.04(2H, d, J=7.3Hz), 7.26(1H, dd, J=7.3Hz and 7.4Hz), 7.32(1H, s), 7.35-7.39(4H, m), 7.45(1H, d, J=7.3Hz), 9.99(1H, br.s), 12.22(1H, br.s).

Example 96

4-(2-Chlorophenyl)-2,4,7,8-tetrahydrofurano[3,4-

b]pyrazolo[4,3-e]pyridin-5-one

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 4-chloroacetoacetate in the same manner as in Example 1.

5 MP:>270°C.

Anal. Calcd. for: $C_{14}H_{10}ClN_3O_2 \cdot 2/5 H_2O$: C, 57.02; H, 3.69; N, 14.25.

Found: C, 57.13; H, 3.39; N, 14.38.

MS(FAB): 288 ($M^+ + 1$).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 4.91(2H, dd, J=5.6Hz and 26.6Hz),
10 5.34(1H, s), 7.15-7.24(3H, m), 7.34(1H, s), 7.41(1H, d, J=6.8Hz),
10.31(1H, br.s), 12.20(1H, br.s).

IR(KBr): ν =3167, 2966, 1722, 1637, 1608, 1510, 1026 cm^{-1} .

Example 97

5'-Ethoxycarbonyl-4',7'-dihydro-6'-propyl-
15 spiro[benzo[b]thiophene-3(2H),4'-2'H-pyrazolo[3,4-b]pyridine]-
5-oxide

A solution of 2-methylthiobenzaldehyde (62 g), Meldrum's acid (58.7 g), ethyl 3-ketohexanoate (64.4 g) and ammonium acetate (40 g) in acetic acid (400 mL) was heated under reflux
20 overnight. After the solution was cooled to room temperature, the solvent was evaporated under reduced pressure to give colorless crystals (40.2 g). To a solution of dimethylformamide (26.3 g) in chloroform (100 mL) were added, under ice-cooling, phosphorus oxychloride (33.6 mL) and a
25 solution of the obtained colorless crystals (30 g) in chloroform (200 mL), and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (370 g) solution was added and the mixture was stirred for one hour. The reaction mixture was extracted with chloroform and the solvent
30 was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give colorless crystals. To a solution of the obtained crystals in acetone (500 mL) was

added diammonium cerium nitrate (42 g) and the mixture was stirred for 30 minutes. The solvent was evaporated under reduced pressure and the residue was extracted with ethyl acetate. The solvent was evaporated under reduced pressure to
5 give colorless crystals. To a solution of the obtained colorless crystals in tetrahydrofuran (500 mL) was added metachloroperbenzoic acid (12 g) at -78°C and the mixture was stirred for 30 minutes. An aqueous sodium thiosulfate solution was added, and the mixture was extracted with chloroform. The
10 solvent was evaporated under reduced pressure to give colorless crystals. By recrystallization from ethyl acetate, colorless crystals (15 g) were obtained. To a solution of the obtained colorless crystals in tetrahydrofuran (100 mL) was added lithium diisopropylamide (2.5 eq.) at -78°C . Immediately
15 thereafter, methanol and an aqueous ammonium chloride solution were added. The mixture was extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. To a solution of the obtained oil in pyridine (50 mL) was added hydrazine (4.2 g) and the mixture was stirred with
20 heating for 2 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give title compound (0.8 g) as colorless crystals.

25 MP: 246°C .

Anal. Calcd. for: $\text{C}_{19}\text{H}_{21}\text{N}_3\text{O}_3\text{S}$: C, 61.44; H, 5.70; N, 11.31.

Found: C, 61.58; H, 5.81; N, 11.16.

MS(EI): 371(M^+).

^1H -NMR (400MHz, $\text{DMSO}-d_6$) δ (ppm): 0.70(3H, t, $J=7.3\text{Hz}$),
30 0.96(3H, t, $J=7.3\text{Hz}$), 1.63-1.68(2H, m), 2.67-2.76(2H, m),
3.07(1H, d, $J=14.9\text{Hz}$), 3.64(2H, q, $J=7.3\text{Hz}$), 4.00(1H, d, $J=14.9\text{Hz}$),
7.05-7.09(2H, m), 7.40(1H, dd, $J=7.3\text{Hz}$ and 7.4Hz),
7.50(1H, dd, $J=7.3\text{Hz}$ and 7.4Hz), 7.81(1H, d, $J=7.3\text{Hz}$),

9.83(1H,br.s), 12.11(1H,br.s).

Example 98

Ethyl 4,7-dihydro-4-(2-hydroxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 A solution of 2-methoxybenzaldehyde (15 g), Meldrum's acid (16 g), ethyl 3-ketohexanoate (17.4 g) and ammonium acetate (9.4 g) in acetic acid (110 mL) was heated under reflux overnight. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced
10 pressure to give colorless crystals (8.0 g). To a solution of the obtained colorless crystals (5.2 g) in dichloromethane (150 mL) were added ethanedithiol (20 mL) and aluminum chloride (32 g), and the mixture was stirred for 2 hours. After neutralization with 1N aqueous sodium hydroxide solution,
15 the mixture was extracted with chloroform. The solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give colorless crystals (2.0 g). To a solution of dimethylformamide (1.9 g) in chloroform (10
20 mL) were added phosphorus oxychloride (2.5 mL) and a solution of the obtained crystals in chloroform (20 mL) under ice-cooling, and the mixture was stirred overnight. Under ice-cooling, an aqueous sodium acetate (27 g) solution was added and the mixture was stirred for one hour. The mixture was
25 extracted with chloroform and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give a colorless oil (1.4 g). To a solution of the obtained oil in pyridine (10 mL) was added hydrazine
30 (0.7 g), and the mixture was stirred with heating for 2 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column

chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (0.2 g) as colorless crystals.

MP:177°C

Anal. Calcd. for: $C_{18}H_{21}N_3O_3$: C, 66.04; H, 6.47; N, 12.84.

5 Found: C, 65.96; H, 6.21; N, 12.66.

MS(EI): 327 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.80(3H, t, J=7.3Hz),
0.96(3H, t, J=7.3Hz), 1.56-1.59(2H, m), 2.70-2.80(2H, m),
3.76(2H, q, J=7.3Hz), 5.50(1H, s), 7.28-7.33(3H, m),
10 7.63(1H, dd, J=7.3Hz and 7.4Hz), 7.76(1H, d, J=7.3Hz),
9.64(1H, br.s), 9.68(1H, br.s), 10.12(1H, br.s).

Example 99

Ethyl 4-(2-aminophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

15 To a solution of ethyl 4,7-dihydro-4-(2-nitrophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (1.68 g) in methanol (30 mL) was added 5% palladium-carbon (500 mg), and the mixture was stirred under 10 atm for 3 hours. After removing palladium-carbon by Celite filtration, the solvent
20 was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (120 mg) as colorless crystals.

MP:179°C.

25 Anal. Calcd. for: $C_{18}H_{22}N_4O_2$: C, 66.24; H, 6.79; N, 17.17.

Found: C, 65.96; H, 6.62; N, 17.16.

MS(EI): 326 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.82(3H, t, J=7.3Hz),
0.98(3H, t, J=7.3Hz), 1.58-1.64(2H, m), 2.72-2.78(2H, m),
30 3.78(2H, q, J=7.3Hz), 5.52(1H, s), 6.35-6.38(2H, br.s), 7.28-
7.36(3H, m), 7.58(1H, dd, J=7.3Hz and 7.4Hz), 7.78(1H, d, J=7.3Hz),
9.58(1H, br.s), 11.48(1H, br.s).

Example 100

Ethyl 4-(2-ethylphenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-ethylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner
5 as in Example 25.

MP:186°C.

Anal. Calcd. for: C₂₀H₂₅N₃O₂ 1/5 H₂O: C, 70.03; H, 7.46; N, 12.25.

Found: C, 69.91; H, 7.53; N, 11.98.

MS(EI): 339 (M⁺).

10 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.86(3H, t, J=7.3Hz),
0.94(3H, t, J=7.3Hz), 1.24(3H, t, J=7.3Hz), 1.64(2H, q, J=7.3Hz),
2.64-2.68(1H, m), 2.77-2.86(3H, m), 3.78(2H, q, J=7.3Hz),
5.34(1H, s), 6.98-7.01(3H, m), 7.07-7.10(2H, m), 9.34(1H, s),
11.89(1H, s).

15 **Example 101**

Ethyl 4,7-dihydro-6-propyl-4-(2-propylphenyl)-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-propylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
20 in the same manner as in Example 25.

MP:197°C.

Anal. Calcd. for: C₂₁H₂₇N₃O₂: C, 71.36; H, 7.70; N, 11.89.

Found: C, 71.07; H, 7.73; N, 11.84.

MS(EI): 353 (M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.3Hz), 0.94-
1.00(6H, m), 1.64(2H, q, J=7.3Hz), 2.68-2.80(4H, m),
3.79(2H, q, J=7.3Hz), 5.33(1H, s), 6.98-7.06(5H, m), 9.34(1H, s),
11.88(1H, s).

Example 102

30 Ethyl 4-(2-butylphenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-butylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner

as in Example 25.

MP:175°C.

Anal. Calcd. for: C₂₂H₂₉N₃O₂: C, 71.90; H, 7.95; N, 11.43.

Found: C, 71.50; H, 7.94; N, 11.36.

5 MS(EI): 367(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.3Hz), 0.92-0.97(6H, m), 1.40(2H, q, J=7.3Hz), 1.60-1.66(4H, m), 2.70-2.82(4H, m), 3.80(2H, q, J=7.3Hz), 5.33(1H, s), 6.97-7.06(5H, m), 9.34(1H, s), 11.88(1H, s).

10 **Example 103**

Ethyl 4,7-dihydro-4-(indan-4-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from indan-4-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner

15 as in Example 1.

MP:181-183°C.

Anal. Calcd. for: C₂₁H₂₅N₃O₂: C, 71.77; H, 7.17; N, 11.96.

Found: C, 71.66; H, 7.14; N, 11.88.

MS(EI): 351(M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90(3H, t, J=7.3Hz), 0.90(3H, t, J=7.3Hz), 1.62(2H, m), 1.80-2.10(2H, m), 2.52-3.10(6H, m), 3.77(2H, q, J=7.3Hz), 5.17(1H, s), 6.81(1H, d, J=6.8Hz), 6.91-6.96(2H, m), 7.14(1H, s), 9.33(1H, br.s), 11.87(1H, br.s).

25 **Example 104**

Ethyl 4,7-dihydro-6-propyl-4-(1,2,3,4-tetrahydronaphthalen-5-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Example 105

Ethyl 4-(benzo[b]furan-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 pyrazolo[3,4-b]pyridine-5-carboxylate

Example 106

Ethyl 4-(benzo[b]thiophen-7-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from benzo[b]thiophene-7-aldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:166°C.

5 Anal. Calcd. for: $C_{20}H_{21}N_3O_2S \cdot 2H_2O$: C, 59.53; H, 6.25; N, 10.41.

Found: C, 59.77; H, 6.46; N, 9.95.

MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.74(3, t, J=7.3Hz),
0.97(3H, t, J=7.3Hz), 1.65-1.69(2H, m), 2.70-2.80(2H, m),
10 3.71(2H, q, J=7.3Hz), 5.48(1H, s), 7.11-7.13(2H, m),
7.26(1H, dd, J=7.4Hz and 7.5Hz), 7.39(1H, d, J=5.4Hz),
7.63(1H, d, J=7.3Hz), 7.68(1H, d, J=5.4Hz), 9.57(1H, s),
11.91(1H, s).

Example 107

15 5'-Ethoxycarbonyl-4',7'-dihydro-6'-propyl-
spiro[benzo[b]thiophene-3(2H),4'-2'H-pyrazolo[3,4-b]pyridine]

To a solution of 5'-ethoxycarbonyl-4',7'-dihydro-6'-propyl-spiro[benzo[b]thiophene-3(2H), 4'-2'H-pyrazolo[3,4-b]pyridine]-1-oxide (100 mg) in carbon tetrachloride (20 mL)
20 was added trimethylsilane iodide (0.1 g), and the mixture was stirred with heating for 30 minutes. The reaction mixture was allowed to cool to ambient temperature, and the mixture was extracted with chloroform. The solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified
25 by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (20 mg) as colorless crystals.

MP:147°C.

Anal. Calcd. for: $C_{19}H_{21}N_3O_2S$: C, 64.20; H, 5.95; N, 11.82.

30 Found: C, 64.18; H, 6.14; N, 11.56.

MS(EI): 355 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.73(3H, t, J=7.3Hz),
0.95(3H, t, J=7.3Hz), 1.64-1.67(2H, m), 2.56-2.64(2H, m),

3.03(1H,d,J=10.2Hz), 3.72(2H,q,J=7.3Hz), 4.03(1H,d,J=10.2Hz),
6.69(1H,d,J=7.3Hz), 6.91(1H,dd,J=7.3Hz and 7.4Hz),
7.03(1H,dd,J=7.3Hz and 7.4Hz), 7.08(1H,s), 7.15(1H,d,J=7.3Hz),
9.65(1H,br.s), 11.96(1H,br.s).

5 **Example 108**

Ethyl 4,7-dihydro-4-methyl-4-phenyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 5'-ethoxycarbonyl-4',7'-dihydro-6'-propyl-spiro[benzo[b]thiophene-3(2H), 4'-2'H-pyrazolo[3,4-b]pyridin]-1-oxide (100 mg) in tetrahydrofuran (10 mL) were
10 added disodium hydrogenphosphate (1.2 g) and methanol (5 mL) under ice-cooling, and 10% sodium amalgam (3.0 g) was added. The mixture was stirred for 5 hours, filtered through Celite and extracted with chloroform. The solvent was evaporated
15 under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (8:2)) to give the title compound (80 mg) as colorless crystals.

MP:207°C.

20 Anal. Calcd. for: C₁₉H₂₃N₃O₂: C, 70.13; H, 7.12; N, 12.91.

Found: C, 69.89; H, 7.18; N, 12.99.

MS(EI): 325(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.71(3H,t,J=7.3Hz),
0.96(3H,t,J=7.3Hz), 1.64-1.68(2H,m), 2.28(3H,s), 2.48-
25 2.56(2H,m), 3.71(2H,q,J=7.3Hz), 6.73-7.01(5H,m), 7.10(1H,s),
9.71(1H,br.s), 11.87(1H,br.s).

Example 109

Ethyl 4,7-dihydro-6-propyl-4-(2,3,5-trichlorophenyl)-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 2,3,5-trichlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:218-220°C (decomposition).

Anal. Calcd. for: $C_{18}H_{18}Cl_3N_3O_2$: C, 52.13; H, 4.37; N, 10.13.

Found: C, 51.76; H, 4.37; N, 10.07.

MS(EI): 414 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=6.9Hz),
5 0.97(3H, t, J=7.3Hz), 1.62-1.67(2H, m), 2.65-2.71(1H, m), 2.85-
2.92(1H, m), 3.76-3.88(2H, m), 5.62(1H, s), 7.03(1H, d, J=1.6Hz),
7.33(1H, s), 7.59(1H, d, J=2.4Hz), 9.69(1H, s), 12.12(1H, s).

Example 110

Ethyl 4,7-dihydro-6-propyl-4-(2,3,4,5-
10 tetrahydrobenzo[b]oxepin-9-yl)-2H-pyrazolo[3,4-b]pyridine-5-
carboxylate

Example 111

Ethyl 4-(3-chloro-2-methylphenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

15 The title compound was prepared from 3-chloro-2-
methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate
in the same manner as in Example 1.

MP: 185°C.

Anal. Calcd. for: $C_{19}H_{22}ClN_3O_2$: C, 63.42; H, 6.16; N, 11.68.

20 Found: C, 63.37; H, 6.12; N, 11.65.

MS(EI): 359 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.87(3H, t, J=7.3Hz),
0.95(3H, t, J=7.3Hz), 1.60-1.66(2H, m), 2.67-2.69(1H, m), 2.74-
2.78(1H, m), 3.78(2H, q, J=7.3Hz), 5.39(1H, s), 6.95(1H, d, J=7.3Hz),
25 7.04(1H, dd, J=7.3Hz and 7.4Hz), 7.12(1H, d, J=7.3Hz), 7.24(1H, s),
9.44(1H, br.s), 11.94(1H, br.s).

Example 112

Ethyl 4-(2,1,3-benzothiadiazol-4-yl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 2,1,3-
benzothiadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-
ketohexanoate in the same manner as in Example 25.

MP: 180°C.

Anal. Calcd. for: $C_{18}H_{19}N_5O_2S$: C, 58.52; H, 5.18; N, 18.96.

Found: C, 58.51; H, 5.19; N, 18.81.

MS(EI): 369 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.62(3H, t, J=7.3Hz),
5 1.00(3H, t, J=7.3Hz), 1.68-1.72(2H, m), 2.76-2.89(2H, m),
3.72(2H, q, J=7.3Hz), 6.02(1H, s), 7.16(1H, s), 7.20(1H, d, J=7.3Hz),
7.60(1H, dd, J=7.3Hz and 7.4Hz), 7.83(1H, d, J=7.3Hz), 9.55(1H, s),
11.89(1H, s).

Example 113

10 Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl acetoacetate in the same manner as in Example 25.

15 MP: 228°C.

Anal. Calcd. for: $C_{16}H_{15}N_5O_3$: C, 59.07; H, 4.65; N, 21.53.

Found: C, 58.85; H, 4.75; N, 21.17.

MS(EI): 325 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.75(3H, t, J=7.3Hz), 2.42(3H, s),
20 3.79(2H, q, J=7.3Hz), 5.67(1H, s), 7.14(1H, d, J=6.6Hz),
7.23(1H, s), 7.49(1H, dd, J=9.0Hz and 6.6Hz), 7.78(1H, d, J=9.0Hz),
9.69(1H, s), 12.02(1H, s).

Example 114

25 Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl benzoylacetate in the same manner as in Example 1.

MP: 190°C.

30 Anal. Calcd. for: $C_{21}H_{17}N_5O_3$: C, 65.11; H, 4.42; N, 18.08.

Found: C, 64.99; H, 4.59; N, 18.06.

MS(EI): 387 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.54(3H, t, J=7.3Hz),

3.56(2H,q,J=7.3Hz), 5.68(1H,s), 7.24(1H,s), 7.26-7.42(6H,m),
7.72(1H,dd,J=7.3Hz and 7.2Hz), 7.94(1H,d,J=7.3Hz),
9.71(1H,s),12.08(1H,s).

Example 115

5 Ethyl 4-(2,3-dichlorophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2,3-dichlorobenzaldehyde, 3-aminopyrazole and ethyl benzoylacetate in the same manner as in Example 1.

10 MP:214°C.

Anal. Calcd. for: C₂₁H₁₇N₅O₃: C, 65.11; H, 4.42; N, 18.08.

Found: C, 64.85; H, 4.48; N, 17.92.

MS(EI): 387(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.57(3H,t,J=7.3Hz),

15 3.52(2H,q,J=7.3Hz), 5.70(1H,s), 7.30-7.40(9H,m), 9.61(1H,s),
12.12(1H,s).

Example 116

(+)Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The compound described in Example 76 was separated using a semi-preparative column for optical resolution (CHIRALPAK AS, 1.0 cm×25 cm, eluent n-hexane/2-propanol/diethylamine=90/10/0.1, flow rate 2.0 mL/min, UV 254 nm, retention time 40 minutes, DAICEL CHEMICAL INDUSTRIES,
25 LTD.) to give the title compound as colorless crystals.

MP: 159°C.

MS(EI): 353(M⁺).

Specific rotation: [α]_D=+260°(EtOH,c=0.5).

Example 117

30 (-)Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The compound described in Example 76 was separated using a semi-preparative column for optical resolution (CHIRALPAK AS,

1.0 cm×25 cm, eluent n-hexane/2-propanol/diethylamine=90/10/0.1, flow rate 2.0 mL/min, UV 254 nm, retention time 55 minutes, DAICEL CHEMICAL INDUSTRIES, LTD.) to give the title compound as colorless crystals.

5 MP: 160°C.

MS(EI): 353(M⁺).

Specific rotation: $[\alpha]_D = -277^\circ$ (EtOH, c=0.5).

Example 118

4-(2-Bromophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butyraldehyde, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP: 226°C.

15 Anal. Calcd. for: C₁₅H₁₅BrN₄O₂: C, 49.60; H, 4.16; N, 15.43.

Found: C, 49.57; H, 4.28; N, 14.96.

MS(EI): 363(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.02(3H, t, J=7.3Hz), 1.72-1.76(2H, m), 2.85-3.05(2H, m), 5.89(1H, s), 7.07-7.1(2H, m),
20 7.25(1H, dd, J=7.5Hz and 7.4Hz), 7.47(1H, s), 7.56(1H, d, J=7.3Hz), 10.84(1H, s), 12.43(1H, s).

Example 119

4,7-Dihydro-4-(2-methoxyphenyl)-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from n-butyraldehyde, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP: 223°C.

Anal. Calcd. for: C₁₆H₁₆N₄O₃: C, 61.13; H, 5.77; N, 17.82.

30 Found: C, 61.01; H, 5.87; N, 17.92.

MS(EI): 314(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.03(3H, t, J=7.3Hz), 1.72-1.78(2H, m), 2.82-3.04(2H, m), 3.86(3H, s), 5.76(1H, s),

6.78(1H,dd,J=7.5Hz and 7.4Hz), 6.90(1H,d,J=7.3Hz),
6.95(1H,d,J=7.3Hz), 7.10(1H,dd,J=7.5Hz and 7.4Hz), 7.33(1H,s),
10.68(1H,s), 12.29(1H,s).

Example 120

5 4,7-Dihydro-4-(2-methylthiophenyl)-5-nitro-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

10 MP:211°C.

Anal. Calcd. for: C₁₆H₁₈N₄O₂S: C, 58.16; H, 5.49; N, 16.96.

Found: C, 57.94; H, 5.47; N, 16.53.

MS(EI): 330(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.02(3H,t,J=7.3z), 1.71-
15 1.76(2H,m), 2.8-3.00(2H,m), 5.89(1H,s), 6.98(1H,d,J=7.3Hz),
7.03(1H,dd,J=7.5Hz and 7.4Hz), 7.13(1H,dd,J=7.5Hz and 7.4Hz),
7.28(1H,d,J=7.3Hz), 7.41(1H,s), 10.74(1H,s), 12.34(1H,s).

Example 121

20 4,7-Dihydro-5-nitro-4-(2-nitrophenyl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP:204°C.

25 Anal. Calcd. for: C₁₅H₁₅N₅O₄: C, 54.71; H, 4.59; N, 21.27.

Found: C, 54.50; H, 4.77; N, 21.32.

MS(EI): 329(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.01(3H,t,J=7.3Hz), 1.69-
1.74(2H,m), 2.85-2.99(2H,m), 5.67(1H,s), 6.94(1H,d,J=7.3Hz),
30 6.98-7.03(2H,m), 7.09(1H,d,J=7.3Hz), 7.38(1H,s), 10.69(1H,s),
12.34(1H,s).

Example 122

4-(2,3-Dichlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-

pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

5 MP:239°C.

Anal. Calcd. for: C₁₅H₁₄Cl₂N₄O₂: C, 51.01; H, 4.00; N, 15.86.

Found: C, 50.70; H, 4.06; N, 15.60.

MS(EI): 353(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.02(3H, t, J=7.3Hz), 1.70-
10 1.74(2H, m), 2.89-2.92(1H, m), 2.96-3.02(1H, m), 5.96(1H, s),
7.09(1H, d, J=7.3Hz), 7.24(1H, dd, J=7.5Hz and 7.4Hz),
7.43(1H, d, J=7.3Hz), 7.49(1H, s), 10.98(1H, s), 12.49(1H, s).

Example 123

4,7-Dihydro-4-(naphthalen-1-yl)-5-nitro-6-propyl-2H-

15 pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, naphthalen-1-aldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP:226°C.

20 Anal. Calcd. for: C₁₉H₁₈N₄O₂: C, 68.25; H, 5.43; N, 16.76.

Found: C, 68.29; H, 5.20; N, 16.67.

MS(EI): 334(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.06(3H, t, J=7.3Hz), 1.76-
1.82(2H, m), 2.95-3.06(2H, m), 6.33(1H, s), 7.18-7.22(2H, m),
25 7.36(1H, dd, J=7.5Hz and 7.4Hz), 7.54(1H, dd, J=7.5Hz and 7.4Hz),
7.60(1H, dd, J=7.5Hz and 7.4Hz), 7.71(1H, d, J=7.3Hz),
7.92(1H, d, J=7.3Hz), 8.46(1H, d, J=7.3Hz), 10.80(1H, s),
12.29(1H, s).

Example 124

30 4,7-Dihydro-4-(3,4-dihydro-2H-benzopyran-8-yl)-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from n-butylaldehyde, 3,4-dihydro-2H-benzopyran-8-aldehyde and 3-aminopyrazole in

the same manner as in Example 93.

MP:234°C.

Anal. Calcd. for: $C_{18}H_{20}N_4O_3$: C, 63.52; H, 5.92; N, 16.46.

Found: C, 63.22; H, 5.94; N, 16.44.

5 MS(EI): 340(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.02(3H, t, J=7.3Hz), 1.71-1.77(2H, m), 1.92-1.95(2H, m), 2.69-2.73(2H, m), 2.85-3.02(2H, m), 4.23-4.28(2, m), 5.71(1H, s), 6.61-6.67(2H, m), 6.80(1H, d, J=7.3Hz), 7.37(1H, s), 10.64(1H, s), 12.28(1H, s).

10 **Example 125**

4-(2,3-Dichlorophenyl)-4,7-dihydro-6-methyl-5-nitro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from acetaldehyde, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as

15 in Example 93.

MP:>270°C.

Anal. Calcd. for: $C_{13}H_{10}Cl_2N_4O_2$: C, 48.02; H, 3.10; N, 17.23.

Found: C, 48.05; H, 3.12; N, 17.24.

MS(EI): 325(M^+).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.66(3H, s), 5.94(1H, s), 7.13(1H, d, J=7.2Hz), 7.22(1H, dd, J=7.3Hz and 7.2Hz), 7.42(1H, d, J=7.3Hz), 7.50(1H, s), 10.94(1H, s), 12.49(1H, s).

Example 126

4-(2,3-Dichlorophenyl)-6-ethyl-4,7-dihydro-5-nitro-2H-pyrazolo[3,4-b]pyridine

25

The title compound was prepared from propionaldehyde, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

MP:250°C.

30 Anal. Calcd. for: $C_{14}H_{12}Cl_2N_4O_2$: C, 49.58; H, 3.57; N, 16.52.

Found: C, 49.54; H, 3.62; N, 16.73.

MS(EI): 339(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.29(3H, t, J=7.3Hz), 2.98-

3.01(2H,m), 5.94(1H,s), 7.10(1H,d,J=7.3Hz), 7.24(1H,dd,J=7.3Hz and 7.2Hz), 7.42(1H,d,J=7.2Hz), 7.49(1H,s), 10.93(1H,s), 12.49(1H,s).

Example 127

5 6-Butyl-4-(2,3-dichlorophenyl)-4,7-dihydro-5-nitro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from pentylaldehyde, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 93.

10 MP:220°C.

Anal. Calcd. for: C₁₆H₁₆Cl₂N₄O₂: C, 52.33; H, 4.39; N, 15.26.

Found: C, 52.64; H, 4.61; N, 14.51.

MS(EI): 367(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H,t,J=7.3Hz), 1.41-
15 1.46(2H,m), 1.63-1.68(2H,m), 2.94-3.04(2H,m), 5.95(1H,s),
7.08(1H,d,J=7.2Hz), 7.23(1H,dd,J=7.3Hz and 7.2Hz),
7.42(1H,d,J=7.2Hz), 7.48(1H,s), 10.97(1H,s), 12.28(1H,s).

Example 128

20 4-(2-Bromophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:237°C.

25 Anal. Calcd. for: C₁₆H₁₅BrN₄: C, 55.99; H, 4.41; N, 16.32.

Found: C, 55.97; H, 4.45; N, 16.40.

MS(EI): 343(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.95(3H,t,J=7.3Hz), 1.64-
1.70(2,m), 2.40-2.44(2H,m), 5.35(1H,s), 7.15(1H,dd,J=7.5Hz and
30 7.4Hz), 7.22(1H,d,J=7.3Hz), 7.27(1H,s), 7.36(1H,dd,J=7.5Hz and
7.4Hz), 7.59(1H,d,J=7.3Hz), 9.84(1H,s), 12.16(1H,s).

Example 129

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-

pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

5 MP:203°C.

Anal. Calcd. for: C₁₇H₁₈N₄O: C, 69.37; H, 6.16; N, 19.03.

Found: C, 69.34; H, 6.25; N, 19.01.

MS(EI): 294(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.96(3H, t, J=7.3Hz), 1.65-
10 1.70(2H, m), 2.38-2.43(2H, m), 3.83(3H, s), 5.22(1H, s),
6.89(1H, dd, J=7.5Hz and 7.4Hz), 6.99(1H, d, J=7.3Hz),
7.05(1H, d, J=7.3Hz), 7.15-7.18(2H, m), 9.65(1H, s), 12.02(1H, s).

Example 130

5-Cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-propyl-2H-

15 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:216°C.

20 Anal. Calcd. for: C₁₇H₁₈N₄S: C, 65.78; H, 5.84; N, 18.05.

Found: C, 65.68; H, 5.81; N, 17.83.

MS(EI): 310(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.96(3H, t, J=7.3Hz), 1.65-
1.70(2H, m), 2.40-2.46(2H, m), 2.48(3H, s), 5.34(1H, s), 7.13-
25 7.21(4H, m), 7.30(1H, d, J=7.3Hz), 9.75(1H, s), 12.07(1H, s).

Example 131

5-Cyano-4,7-dihydro-4-(2-methylphenyl)-6-propyl-2H-pyrazolo
[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
30 2-methylbenzaldehyde and 3-aminopyrazole in the same manner as
in Example 94.

MP:230°C.

Anal. Calcd. for: C₁₇H₁₈N₄: C, 73.35; H, 6.52; N, 20.13.

Found: C, 73.44; H, 6.61; N, 20.13.

MS(EI): 278(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.93(3H, t, J=7.3Hz), 1.65-
1.67(2H, m), 2.32(3H, s), 2.35-2.41(2H, m), 5.13(1H, s), 7.06-
5 7.16(5H, m), 9.69(1H, s), 12.07(1H, s).

Example 132

5-Cyano-4,7-dihydro-4-(2-nitrophenyl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
10 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as
in Example 94.

MP: 216°C.

Anal. Calcd. for: C₁₆H₁₅N₅O₂: C, 62.13; H, 4.89; N, 22.64.

Found: C, 62.16; H, 4.93; N, 22.57.

15 MS(EI): 309(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.64-
1.69(2H, m), 2.36-2.42(2H, m), 5.38(1H, s), 7.27(1H, s), 7.42-
7.49(2H, m), 7.70(1H, dd, J=7.5Hz and 7.4Hz), 7.89(1H, d, J=7.3Hz),
9.91(1H, s), 12.21(1H, s).

20 **Example 133**

5-Cyano-4-(2-cyanophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
2-cyanobenzaldehyde and 3-aminopyrazole in the same manner as
25 in Example 94.

MP: 218°C.

Anal. Calcd. for: C₁₇H₁₅N₅: C, 70.57; H, 5.23; N, 24.21.

Found: C, 70.54; H, 5.30; N, 24.07.

MS(EI): 289(M⁺).

30 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.63-
1.68(2H, m), 2.36-2.40(2H, m), 5.23(1H, s), 7.26(1H, s),
7.38(1H, d, J=7.3Hz), 7.43(1H, dd, J=7.5Hz and 7.4Hz),
7.69(1H, dd, J=7.5Hz and 7.4Hz), 7.80(1H, d, J=7.3Hz), 9.94(1H, s),

12.22(1H,s).

Example 134

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl butanoate, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:242°C.

Anal. Calcd. for: C₁₆H₁₄Cl₂N₄ 1/5 H₂O: C, 57.05; H, 4.31; N, 16.63.

10 Found: C, 57.23; H, 4.49; N, 16.25.

MS(EI): 333(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.62-1.68(2H, m), 2.40-2.46(2H, m), 5.44(1H, s), 7.22(1H, d, J=7.3Hz), 7.30(1H, s), 7.35(1H, dd, J=7.5Hz and 7.4Hz), 7.51(1H, d, J=7.3Hz),
15 9.89(1H, s), 12.19(1H, s).

Example 135

5-Cyano-4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl butanoate, naphthalene-1-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:263°C.

Anal. Calcd. for: C₂₀H₁₆N₄: C, 76.41; H, 5.77; N, 17.82.

Found: C, 76.05; H, 5.85; N, 17.73.

25 MS(EI): 314(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.97(3H, t, J=7.3Hz), 1.68-1.73(2H, m), 2.44-2.48(2H, m), 5.71(1H, s), 7.04(1H, s), 7.39-7.46(4H, m), 7.81(1H, d, J=7.3Hz), 7.94(1H, d, J=7.3Hz), 9.83(1H, s), 12.02(1H, s).

30 **Example 136**

5-Cyano-4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,

3,4-dihydro-2H-benzopyran-8-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:230°C.

Anal. Calcd. for: $C_{19}H_{20}N_4O$: C, 71.23; H, 6.29; N, 17.49.

5 Found: C, 71.20; H, 6.48; N, 17.55.

MS(EI): 320 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, J=7.3Hz), 1.64-1.70(2H, m), 1.92-1.95(2H, m), 2.38-2.43(2H, m), 2.72-2.76(2H, m), 4.16-4.27(2H, m), 5.16(1H, s), 6.74(1H, dd, J=7.5Hz and 7.4Hz),
10 6.83-6.88(2H, m), 7.20(1H, s), 9.62(1H, s), 12.01(1H, s).

Example 137

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
15 2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:194°C.

Anal. Calcd. for: $C_{16}H_{14}N_6O$: C, 62.73; H, 4.61; N, 27.44.

Found: C, 62.52; H, 4.78; N, 27.19.

20 MS(EI): 306 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, J=7.3Hz), 1.63-1.68(2H, m), 2.38-2.43(2H, m), 5.40(1H, s), 7.25(1H, s), 7.40(1H, d, J=7.3Hz), 7.58(1H, dd, J=7.5Hz and 7.4Hz), 7.92(1H, d, J=7.3Hz), 9.93(1H, s), 12.13(1H, s).

25 Example 138

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
2,1,3-benzothiadiazol-4-aldehyde and 3-aminopyrazole in the
30 same manner as in Example 94.

MP:195°C.

Anal. Calcd. for: $C_{16}H_{14}N_6S$: C, 59.61; H, 4.38; N, 26.07.

Found: C, 59.33; H, 4.48; N, 25.76.

MS(EI):322(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.98(3H,t,J=7.3Hz), 1.68-
1.74(2H,m), 2.45-2.50(2H,m), 5.72(1H,s), 7.19(1H,s),
7.43(1H,d,J=7.3Hz), 7.72(1H,dd,J=7.5Hz and 7.4Hz),
5 7.97(1H,d,J=7.3Hz), 9.87(1H,s), 12.06(1H,s).

Example 139

5-Cyano-4,7-dihydro-4-(2-methylbenzoxazol-4-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
10 2-methylbenzoxazole-4-aldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:208°C.

Anal. Calcd. for:C₁₈H₁₇N₅O 1/5 H₂O:C,66.94;H,5.43;N,21.68.

Found:C,66.85;H,5.52;N,22.09.

15 MS(EI):319(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.97(3H,t,J=7.3Hz), 1.67-
1.72(2H,m), 2.40-2.45(2H,m), 2.63(3H,s), 5.51(1H,s),
7.06(1H,d,J=7.3Hz), 7.16(1H,s), 7.29(1H,dd,J=7.3Hz and 7.2Hz),
7.47(1H,d,J=7.3Hz), 9.77(1H,s), 12.06(1H,s).

20 **Example 140**

R(-) 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

To a solution of the compound described in Example 137
(64.5 g) in THF (1000 mL) was added (-)camphorsulfonic acid
25 (49 g) at room temperature and the mixture was stirred for 1
hour. The solvent was evaporated under reduced pressure to
give an oil. The obtained oil was recrystallized from
acetonitrile twice to give colorless crystals (11 g). To a
solution of the obtained colorless crystals in methanol (50
30 mL) was added water (50 mL). The mixture was neutralized with
a saturated aqueous sodium hydrogencarbonate solution and
extracted with ethyl acetate. The solvent was evaporated under
reduced pressure. The residual methanol solution was added

dropwise to water (1000 mL) and the crystals were collected by filtration to give the title compound (11 g) as pale-yellow crystals.

(CHIRALPAK AS, 0.25 cm×25 cm, eluent n-hexane/2-

5 propanol/diethylamine =80/20/0.1, flow rate 1.5 mL/min, UV 254 nm, retention time 10 minutes, DAICEL CHEMICAL INDUSTRIES, LTD.)

MP: 170°C.

MS(EI): 306(M⁺).

10 Specific rotation: $[\alpha]_D = -80^\circ$ (EtOH, c=1.0).

Example 141

S(+) 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

To a solution of the compound (54 g), which was
15 recovered from the mother liquor obtained in Example 140, in THF (600 mL) was added (+)camphorsulfonic acid (41 g) at room temperature and the mixture was stirred for 1 hour. The solvent was evaporated under reduced pressure to give an oil. The obtained oil was recrystallized from acetonitrile twice to
20 give colorless crystals (12 g). To a solution of the obtained colorless crystals in methanol (50 mL) was added water (50 mL). The mixture was neutralized with a saturated aqueous sodium hydrogencarbonate solution and extracted with ethyl acetate. The solvent was evaporated under reduced pressure and the
25 residual methanol solution was added dropwise to water (1000 mL). The crystals were collected by filtration to give the title compound (11 g) as pale-yellow crystals.

(CHIRALPAK AS, 0.25 cm×25 cm, eluent n-hexane/2-

30 propanol/diethylamine =80/20/0.1, flow rate 1.5 mL/min, UV 254 nm, retention time 13 minutes, DAICEL CHEMICAL INDUSTRIES, LTD.)

MP: 170°C.

MS(EI): 306(M⁺).

Specific rotation: $[\alpha]_D = +82^\circ$ (EtOH, $c=1.0$).

Example 142

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl benzoate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:158°C.

Anal. Calcd. for: $C_{19}H_{13}ClN_4$ H_2O : C, 65.05; H, 4.31; N, 15.97.

10 Found: C, 65.35; H, 4.19; N, 16.21.

MS(EI): 332 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.51(1H, s), 7.25-7.51(8H, m), 7.59-7.61(2H, m), 10.07(1H, s), 12.24(1H, s).

Example 143

15 5-Cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

20 MP:146°C.

Anal. Calcd. for: $C_{20}H_{16}N_4S$ $4/5 H_2O$: C, 66.94; H, 4.94; N, 15.61.

Found: C, 66.85; H, 4.81; N, 15.65.

MS(EI): 344 (M^+).

25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.48(3H, s), 5.48(1H, s), 7.19-7.33(5H, m), 7.48-7.50(3H, m), 7.59-7.61(2H, m), 9.99(1H, s), 12.16(1H, s).

Example 144

5-Cyano-4-(2-cyanophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl benzoate, 2-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:148°C.

Anal. Calcd. for: $C_{20}H_{13}N_5 \cdot 3/5 H_2O$: C, 71.89; H, 4.28; N, 20.96.

Found: C, 71.89; H, 4.33; N, 20.91.

MS(EI): 323 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.38(1H, s), 7.31(1H, s), 7.44-
5 7.59(7H, m), 7.70(1H, dd, J=7.3Hz and 7.2Hz), 7.83(1H, d, J=7.3Hz),
10.21(1H, s), 12.31(1H, s).

Example 145

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-phenyl-2H-
pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl benzoate,
2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 95.

MP: 162°C.

Anal. Calcd. for: $C_{19}H_{12}Cl_2N_4$: C, 62.14; H, 3.29; N, 15.26.

15 Found: C, 61.57; H, 3.93; N, 17.19.

MS(EI): 367 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.59(1H, s), 7.37-7.42(3H, m),
7.48-7.55(4H, m), 7.59-7.62(2H, m), 10.14(1H, s), 12.28(1H, s).

Example 146

20 5-Cyano-4,7-dihydro-4-(naphthalen-1-yl)-6-phenyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate,
naphthalene-1-benzaldehyde and 3-aminopyrazole in the same
manner as in Example 95.

25 MP: 174°C.

Anal. Calcd. for: $C_{23}H_{16}N_4$: C, 79.29; H, 4.63; N, 16.08.

Found: C, 79.50; H, 4.85; N, 16.58.

MS(EI): 348 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.87(1H, s), 7.12(1H, s), 7.50-
30 7.63(9H, m), 7.82(1H, d, J=7.3Hz), 7.96(1H, d, J=7.3Hz),
8.34(1H, d, J=7.3Hz), 10.09(1H, s), 12.12(1H, s).

Example 147

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-

pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

5 MP:>270°C.

Anal. Calcd. for: C₂₀H₁₂BrN₅: C, 59.72; H, 3.01; N, 17.41.

Found: C, 59.53; H, 3.17; N, 17.30.

MS(EI): 402(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.63(1H, s), 7.39(1H, s), 7.49-
10 7.51(3H, m), 7.60-7.63(3H, m), 7.75(1H, d, J=7.3Hz),
7.85(1H, d, J=7.3Hz), 10.21(1H, s), 12.33(1H, s).

Example 1485-Cyano-4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from methyl benzoate, 3,4-dihydro-2H-benzopyran-8-benzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:255°C.

Anal. Calcd. for: C₂₂H₁₈N₄O: C, 74.56; H, 5.12; N, 15.81.

20 Found: C, 74.27; H, 5.11; N, 15.82.

MS(EI): 354(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.94-1.97(2H, m), 2.75-2.78(2H, m),
4.20-4.30(2H, m), 5.30(1H, s), 6.80(1H, dd, J=7.3Hz and 7.2Hz),
6.91(1H, d, J=7.3Hz), 7.02(1H, d, J=7.3Hz), 7.28(1H, s), 7.49-
25 7.51(3H, m), 7.60-7.63(2H, m), 9.88(1H, s), 12.11(1H, s).

Example 1495-Cyano-4-(2,3-difluorophenyl)-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate,
30 2,3-difluorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:165°C.

Anal. Calcd. for: C₁₉H₁₂F₂N₄ 3/5 H₂O: C, 66.12; H, 3.86; N, 16.23.

Found: C, 65.87; H, 3.81; N, 16.46.

MS(EI): 334 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 5.40(1H, s), 7.16-7.38(4H, m), 7.48-7.50(3H, m), 7.57-7.59(2H, m), 10.11(1H, s), 12.30(1H, s).

5 **Example 150**

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as
10 in Example 95.

MP: 206°C.

Anal. Calcd. for: $\text{C}_{20}\text{H}_{16}\text{N}_4\text{O}$: C, 73.15; H, 4.91; N, 17.06.

Found: C, 73.23; H, 5.14; N, 17.19.

MS(EI): 328 (M^+).

15 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 3.86(3H, s), 5.36(1H, s), 6.94(1H, dd, $J=7.3\text{Hz}$ and 7.2Hz), 7.02(1H, d, $J=7.3\text{Hz}$), 7.19-7.25(3H, m), 7.48-7.51(3H, m), 7.60-7.63(2H, m), 9.91(1H, s), 12.12(1H, s).

Example 151

20 5-Cyano-4,7-dihydro-4,6-bis(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl o-anisate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

25 MP: 220°C.

Anal. Calcd. for: $\text{C}_{21}\text{H}_{18}\text{N}_4\text{O}_2$: C, 70.38; H, 5.06; N, 15.63.

Found: C, 69.97; H, 5.13; N, 16.15.

MS(EI): 358 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 3.86(3H, s), 3.88(3H, s),
30 5.32(1H, s), 6.95-7.06(3H, m), 7.14-7.25(3H, m), 7.37(1H, d, $J=7.3\text{Hz}$), 7.45(1H, dd, $J=7.3\text{Hz}$ and 7.2Hz), 9.74(1H, s), 12.05(1H, s).

Example 152

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(3-methoxyphenyl)-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl m-anisate,
2-methoxybenzaldehyde and 3-aminopyrazole in the same manner
5 as in Example 95.

MP:192°C.

Anal. Calcd. for: C₂₁H₁₈N₄O₂: C, 70.38; H, 5.06; N, 15.63.

Found: C, 69.97; H, 5.09; N, 15.54.

MS(EI): 358(M⁺).

10 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.81(3H, s), 3.86(3H, s),
5.35(1H, s), 6.95(1H, dd, J=7.3Hz and 7.2Hz), 7.01(1H, d, J=7.3Hz),
7.07(1H, d, J=7.3Hz), 7.14(1H, s), 7.18-7.23(5H, m),
7.41(1H, dd, J=7.3Hz and 7.2Hz), 9.88(1H, s), 12.12(1H, s).

Example 153

15 5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(4-methoxyphenyl)-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl p-anisate,
2-methoxybenzaldehyde and 3-aminopyrazole in the same manner
as in Example 95.

20 MP:149°C.

Anal. Calcd. for: C₂₁H₁₈N₄O₂ 1/2 H₂O: C, 68.65; H, 5.21; N, 15.25.

Found: C, 68.67; H, 4.99; N, 15.35.

MS(EI): 358(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.81(3H, s), 3.86(3H, s),
25 5.33(1H, s), 6.94(1H, dd, J=7.3Hz and 7.2Hz), 7.01-7.05(3H, m),
7.18-7.24(3H, m), 7.56(2H, d, J=7.2Hz), 9.82(1H, s), 12.10(1H, s).

Example 154

5-Cyano-4,7-dihydro-4-(2-nitrophenyl)-6-phenyl-2H-
pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl benzoate, 2-
nitrobenzaldehyde and 3-aminopyrazole in the same manner as in
Example 95.

MP:221°C.

Anal. Calcd. for: $C_{19}H_{13}N_5O_2$: C, 66.47; H, 3.82; N, 20.40.

Found: C, 66.48; H, 4.08; N, 20.41.

MS(EI): 343(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54(1H, s), 7.34(1H, s), 7.49-
5 7.52(4H, m), 7.59-7.64(3H, m), 7.74(1H, dd, J=7.3Hz and 7.2Hz),
7.91(1H, d, J=7.3Hz), 10.16(1H, s), 12.30(1H, s).

Example 155

5-Cyano-4,7-dihydro-6-(2-methoxyphenyl)-4-(2-nitrophenyl)-2H-
pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl o-anisate,
2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as
in Example 95.

MP: 207°C.

Anal. Calcd. for: $C_{20}H_{15}N_5O_3$: C, 64.34; H, 4.05; N, 18.76.

15 Found: C, 64.03; H, 4.21; N, 18.68.

MS(EI): 373(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.85(3H, s), 5.50(1H, s),
7.03(1H, dd, J=7.3Hz and 7.2Hz), 7.14(1H, d, J=7.3Hz), 7.33(1H, s),
7.37(1H, d, J=7.3Hz), 7.44-7.52(2H, m), 7.74-7.80(2H, m),
20 7.92(1H, d, J=7.3Hz), 10.02(1H, s), 12.25(1H, s).

Example 156

5-Cyano-4,7-dihydro-6-(3-methoxyphenyl)-4-(2-nitrophenyl)-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl m-anisate,
25 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as
in Example 95.

MP: 220°C.

Anal. Calcd. for: $C_{20}H_{15}N_5O_3$: C, 64.34; H, 4.05; N, 18.76.

Found: C, 63.92; H, 4.14; N, 18.74.

30 MS(EI): 373(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 3.81(3H, s), 5.53(1H, s),
7.07(1H, d, J=7.3Hz), 7.14-7.18(2H, m), 7.33(1H, s),
7.40(1H, dd, J=7.3Hz and 7.2Hz), 7.50(1H, dd, J=7.3Hz and 7.2Hz),

7.63(1H,d,J=7.3Hz), 7.74(1H,dd,J=7.3Hz 7.2Hz),
7.91(1H,d,J=7.3Hz), 10.13(1H,s), 12.30(1H,s).

Example 157

5-Cyano-4,7-dihydro-6-(4-methoxyphenyl)-4-(2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl p-anisate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:215°C.

Anal. Calcd. for: C₂₀H₁₅N₅O₃: C, 64.34; H, 4.05; N, 18.76.

Found: C, 64.13; H, 4.12; N, 18.69.

MS(EI): 373(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.81(3H,s), 5.51(1H,s),
7.03(2H,d,J=7.3Hz), 7.33(1H,s), 7.47-7.55(3H,m), 7.61(1H,d),
7.74(1H,dd,J=7.3Hz and 7.2Hz), 7.91(1H,d,J=7.3Hz), 10.07(1H,s),
12.28(1H,s).

Example 158

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:231°C.

Anal. Calcd. for: C₁₉H₁₂N₆O: C, 67.05; H, 3.55; N, 24.69.

Found: C, 66.76; H, 3.90; N, 24.71.

MS(EI): 340(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.55(1H,s), 7.33(1H,s), 7.50-7.64(7H,m), 7.95(1H,d,J=7.3Hz), 10.20(1H,s), 12.23(1H,s).

Example 159

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl o-anisate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the

same manner as in Example 95.

MP:180°C.

Anal. Calcd. for: C₂₀H₁₄N₆O₂: C, 64.86; H, 3.81; N, 22.69.

Found: C, 64.11; H, 3.98; N, 22.34.

5 MS(EI): 370(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.84(3H, s), 5.56(1H, s),
7.03(1H, dd, J=7.3Hz and 7.2Hz), 7.14(1H, d, J=6.8Hz), 7.33-
7.35(2H, m), 7.45(1H, dd, J=7.3Hz and 7.2Hz), 7.54(1H, d, J=7.3Hz),
7.65(1H, dd, J=8.8Hz and 6.8Hz), 7.94(1H, d, J=8.8Hz), 10.04(1H, s),
10 12.18(1H, s).

Example 160

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(3-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl m-anisate,
15 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:198°C.

Anal. Calcd. for: C₂₀H₁₄N₆O₂ 4/5 H₂O: C, 62.43; H, 4.09; N, 21.84.

Found: C, 62.60; H, 3.99; N, 22.15.

20 MS(EI): 370(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.80(3H, s), 5.55(1H, s), 7.06-
7.17(3H, m), 7.33(1H, s), 7.40(1H, dd, J=7.3Hz),
7.52(1H, d, J=6.6Hz), 7.62(1H, dd, J=8.8Hz and 6.8Hz),
7.95(1H, d, J=6.8Hz), 10.18(1H, s), 12.24(1H, s).

25 Example 161

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl p-anisate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
30 same manner as in Example 95.

MP:244°C.

Anal. Calcd. for: C₂₀H₁₄N₆O₂: C, 64.86; H, 3.81; N, 22.69.

Found: C, 64.77; H, 3.91; N, 22.49.

MS(EI):370(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 3.80(3H,s), 5.53(1H,s),
7.02(2H,d,J=7.3Hz), 7.32(1H,s), 7.50-7.53(3H,m),
7.61(1H,dd,J=8.8Hz and 6.8Hz), 7.94(1H,d,J=8.8Hz), 10.11(1H,s),
5 12.21(1H,s).

Example 162

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl benzoate,
10 2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:258°C.

MS(EI):356(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 5.85(1H,s), 7.27(1H,s), 7.51-
15 7.52(3H,m), 7.61-7.67(3H,m), 7.76(1H,dd,J=8.8Hz and 6.8Hz),
8.00(1H,d,J=8.8Hz); 10.13(1H,s), 12.16(1H,s).

Example 163

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-
methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl o-anisate,
2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:231°C.

Anal. Calcd. for:C₂₀H₁₄N₆OS 3/10 H₂O:C,61.30;H,3.76;N,21.45.

25 Found:C,61.24;H,3.74;N,22.09.

MS(EI):386(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 3.89(3H,s),5.85(1H,s),
7.06(1H,dd,J=7.6Hz and 7.3Hz), 7.17(1H,d,J=8.3Hz), 7.28(1H,s),
7.43-7.49(2H,m), 7.69(1H,d,J=6.8Hz), 7.80(1H,dd,J=8.8Hz and
30 6.8Hz), 7.99(1H,d,J=8.8Hz), 9.97(1H,s), 12.11(1H,s).

Example 164

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(3-
methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl m-anisate, 2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:220°C.

5 Anal. Calcd. for: C₂₀H₁₄N₆OS: C, 62.16; H, 3.65; N, 21.75.

Found: C, 61.98; H, 3.70; N, 21.66.

MS(EI): 386(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.82(3H, s), 5.85(1H, s),

7.08(1H, d, J=8.3Hz), 7.19(1H, s), 7.23-7.27(2H, m),

10 7.42(1H, dd, J=7.8Hz and 7.2Hz), 7.61(1H, d, J=6.6Hz),

7.75(1H, dd, J=8.8Hz and 6.8Hz), 7.99(1H, d, J=8.1Hz), 10.10(1H, s),

12.16(1H, s).

Example 165

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl p-anisate, 2,1,3-benzothiadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:238°C.

20 MS(EI): 386(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.81(3H, s), 5.83(1H, s),

7.04(2H, d, J=8.8Hz), 7.26(1H, s), 7.73-7.77(3H, m),

7.75(1H, dd, J=8.8Hz and 6.8Hz), 7.99(1H, d, J=8.8Hz), 10.04(1H, s),

12.14(1H, s).

25 Example 166

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isonicotinate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:236°C.

MS(EI): 341(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.58(1H, s), 7.35(1H, s), 7.54-

7.64(4H,m), 7.96(1H,d,J=8.1Hz), 8.72(2H,d,J=5.9Hz),
10.40(1H,s), 12.29(1H,s).

Example 167

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-pyridin-
5 3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl nicotinate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:216°C.

10 Anal. Calcd. for: C₁₈H₁₁N₇O 1/5 H₂O: C, 62.68; H, 3.33; N, 28.43.

Found: C, 62.73; H, 3.43; N, 28.30.

MS(EI): 341(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.59(1H,s), 7.35(1H,s), 7.52-
7.63(3H,m), 7.95-8.00(2H,m), 8.69(1H,d,J=4.9Hz), 8.76(1H,s),
15 10.39(1H,s), 12.28(1H,s).

Example 168

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(4-pyridin-
2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl picolinate,
20 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:188°C.

MS(EI): 341(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.59(1H,s), 7.34(1H,s), 7.51-
25 7.53(2H,m), 7.63(1H,dd,J=9.0Hz and 6.6Hz), 7.75(1H,d,J=6.6Hz),
7.95-7.97(2H,m), 8.69(1H,d,J=5.4Hz), 10.20(1H,s), 12.26(1H,s).

Example 169

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-
(naphthalen-1-yl)-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl 1-naphthoate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 95.

MP:213°C.

Anal. Calcd. for: $C_{23}H_{14}N_6O$: C, 70.76; H, 3.61; N, 21.53.

Found: C, 70.33; H, 3.74; N, 21.23.

MS(EI): 390 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.65(1H, s), 7.35-7.66(7H, m),
5 7.96-8.21(4H, m), 10.35(1H, s), 12.23(1H, s).

Example 170

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(furan-2-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl furan-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 241°C.

Anal. Calcd. for: $C_{17}H_{10}N_6O_2$: C, 61.82; H, 3.05; N, 25.44.

Found: C, 61.72; H, 3.19; N, 25.34.

15 MS(EI): 330 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54(1H, s), 6.69(1H, s),
7.22(1H, d, J=3.4Hz), 7.32(1H, s), 7.48(1H, d, J=6.3Hz),
7.61(1H, dd, J=9.0Hz and 6.3Hz), 7.89(1H, s), 7.94(1H, d, J=9.0Hz),
10.17(1H, s), 12.26(1H, s).

20 Example 171

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 230°C.

Anal. Calcd. for: $C_{17}H_{10}N_6OS$: C, 58.95; H, 2.91; N, 24.26.

Found: C, 58.71; H, 3.08; N, 24.03.

MS(EI): 346 (M^+).

30 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54(1H, s), 7.17(1H, dd, J=4.9Hz and 4.8Hz), 7.33(1H, s), 7.49(1H, d, J=6.6Hz), 7.58-7.64(2H, m),
7.77(1H, d, J=4.9Hz), 7.95(1H, d, J=9.0Hz), 10.21(1H, s),
12.27(1H, s).

Example 172

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(naphthalen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 2-naphthoate,
5 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:228°C.

Anal. Calcd. for: C₂₃H₁₄N₆O: C, 70.76; H, 3.61; N, 21.53.

Found: C, 70.66; H, 3.81; N, 20.94.

10 MS(EI): 390(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.48(1H, s), 7.24(1H, s), 7.44-7.55(5H, m), 7.85-7.92(4H, m), 8.05(1H, s), 10.21(1H, s), 12.14(1H, s).

Example 173

15 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(furan-2-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl furan-3-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

20 MP:237°C.

Anal. Calcd. for: C₁₇H₁₀N₆O₂: C, 61.82; H, 3.05; N, 25.44.

Found: C, 61.59; H, 3.27; N, 25.01.

MS(EI): 330(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.52(1H, s), 6.93(1H, d, J=1.0Hz),
25 7.31(1H, s), 7.48(1H, d, J=6.6Hz), 7.60(1H, dd, J=9.0Hz and 6.6Hz), 7.80(1H, dd, J=1.0Hz), 7.94(1H, d, J=9.0Hz), 8.24(1H, s), 10.07(1H, s), 12.25(1H, s).

Example 174

30 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-3-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 242°C.

Anal. Calcd. for: C₁₇H₁₀N₆OS: C, 58.95; H, 2.91; N, 24.26.

Found: C, 58.52; H, 3.15; N, 23.92.

MS(EI): 346(M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.54(1H, s), 7.32(1H, s),
7.42(1H, d, J=5.1Hz), 7.50(1H, d, J=6.6Hz), 7.61-7.66(2H, m),
7.94(1H, d, J=9.0Hz), 8.00(1H, s), 10.13(1H, s), 12.24(1H, s).

Example 175

6-(Benzo[b]furan-2-yl)-4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-
10 4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
benzo[b]furan-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde
and 3-aminopyrazole in the same manner as in Example 95.

MP: >270°C.

15 Anal. Calcd. for: C₂₁H₁₂N₆O₂: C, 66.31; H, 3.18; N, 22.09.

Found: C, 66.26; H, 3.34; N, 21.53.

MS(EI): 380(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.62(1H, s), 7.31-7.36(2H, m),
7.45(1H, dd, J=9.0Hz and 6.7Hz), 7.53(1H, d, J=6.7Hz), 7.61-
20 7.65(3H, m), 7.77(1H, d, J=7.3Hz), 7.96(1H, d, J=9.0Hz),
10.44(1H, s), 12.33(1H, s).

Example 176

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-methyl-2H-
pyrazolo[3,4-b]pyridine

25 The title compound was prepared from ethyl acetate,
2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 94.

MP: 212°C.

Anal. Calcd. for: C₁₄H₁₀N₆O 3/5 H₂O: C, 58.17; H, 3.91; N, 29.07.

30 Found: C, 58.45; H, 4.08; N, 28.61.

MS(EI): 278(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.14(3H, s), 5.40(1H, s),
7.25(1H, s), 7.40(1H, d, J=6.6Hz), 7.59(1H, dd, J=9.0Hz 6.6Hz),

7.92(1H,d,J=9.0Hz), 9.98(1H,s), 12.13(1H,s).

Example 177

4-(2,1,3-Benzoxadiazol-4-yl)-6-butyl-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl pentanoate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:200°C.

Anal. Calcd. for: C₁₇H₁₆N₆O: C, 63.74; H, 5.03; N, 26.23.

10 Found: C, 63.85; H, 5.01; N, 26.26.

MS(EI): 320(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H,t,J=7.3Hz), 1.30-1.39(2H,m), 1.57-1.65(2H,m), 2.06-2.40(2H,m), 5.39(1H,s), 7.25(1H,s), 7.39(1H,d,J=6.6Hz), 7.59(1H,dd,J=9.0Hz and 6.6Hz),
15 7.91(1H,d,J=9.0Hz), 9.94(1H,s), 12.13(1H,s).

Example 178

Ethyl 4-(2-chloro-3-methylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

A suspension of 2-chloro-m-xylene (15 ml), N-
20 bromosuccinimide (23.3 g) and benzoyl peroxide (200 mg) in carbon tetrachloride (150 ml) was heated under reflux for 6 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography
25 (eluent: hexane) to give 2-bromomethyl-1-chloro-6-methylbenzene (16.0 g) as a colorless oil. 2-Bromomethyl-1-chloro-6-methylbenzene (25.4 g) and hexamethylenetetramine (32.4 g) were dissolved in acetic acid-water (1:1, 10 ml) and the mixture was heated under reflux for 5 hours. To the
30 reaction mixture was added concentrated hydrochloric acid (40 ml) and the mixture was heated under reflux for 1 hour. The reaction mixture was extracted with ethyl acetate. The extract was washed with an aqueous sodium hydrogencarbonate solution

and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give 2-chloro-3-methylbenzaldehyde (19.4 g) as a yellow oil. Subsequently, the title compound was prepared from 2-chloro-3-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:198-200°C.

Anal. Calcd. for: $C_{19}H_{22}ClN_3O_2$: C, 63.42; H, 6.16; N, 11.68.

Found: C, 63.19; H, 6.14; N, 11.71.

MS(EI): 359 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.85(3H, t, J=7.3Hz), 0.97(3H, t, J=7.3Hz), 1.65(2H, m), 2.33(3H, s), 2.68-2.71(1H, m), 2.79-2.84(1H, m), 3.72-3.82(2H, m), 5.63(1H, s), 6.93-6.96(1H, m), 7.05-7.07(2H, m), 7.24(1H, s), 9.46(1H, s), 11.94(1H, s).

Example 179

Ethyl 4-(2-chloro-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 2-chloro-3-nitrobenzoic acid (5.0 g) in THF (50 ml) was added borane-tetrahydrofuran complex (1M THF solution, 30 ml) under ice-cooling and the mixture was stirred at room temperature for 24 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract was washed with water and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give a pale-yellow solid (3.7 g). The obtained pale-yellow solid (1.6 g) and manganese dioxide (1.7 g) were heated under reflux in toluene for 4.5 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (4:1)) to give 2-chloro-3-nitrobenzaldehyde (1.3 g) as a pale-yellow solid. Subsequently, the title compound

was prepared from 2-chloro-3-nitrobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MS(EI): 390(M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=6.8Hz), 0.97(3H, t, J=7.3Hz), 1.64-1.68(2H, m), 2.70-2.85(2H, m), 3.73-3.86(2H, m), 5.67(1H, s), 7.31(1H, s), 7.39-7.47(2H, m), 7.73(1H, dd, J=1.5, 7.8Hz), 9.67(1H, s), 12.10(1H, s).

Example 180

10 Ethyl 4-(2-chloro-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 2-chloro-3-methylbenzaldehyde (19.4 g) in ethanol (45 ml) was added an aqueous hydroxylamine hydrochloride (9.7 g) solution (12 ml), and an aqueous sodium
15 hydroxide (6.9 g) solution (10 ml) was added. The mixture was stirred at room temperature for 1.5 hours. Water (500 ml) was added and the precipitated crystals were collected by filtration. The obtained white crystals (16.1 g) were dissolved in acetic anhydride (50 ml) and the mixture was
20 heated under reflux for 2.5 hours. The reaction mixture was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (5:1)) to give 2-cyano-6-methylchlorobenzene (10.9 g) as a white solid. A suspension of
25 2-cyano-6-methylchlorobenzene (10.9 g), N-bromosuccinimide (12.8 g) and benzoyl peroxide (523 mg) in carbon tetrachloride (100 ml) was heated under reflux for 3.5 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by
30 silica gel column chromatography (eluent: hexane-ethyl acetate (20:1)) to give 2-chloro-3-cyanobenzaldehyde (12.8 g) as a colorless oil. Subsequently, the title compound was prepared from 2-chloro-3-cyanobenzaldehyde, 3-aminopyrazole and ethyl

3-ketohexanoate in the same manner as in Example 25.

MP: 213–215°C.

Anal. Calcd. for: $C_{19}H_{19}ClN_4O_2$: C, 61.54; H, 5.16; N, 15.11.

Found: C, 61.25; H, 5.36; N, 14.71.

5 MS(EI): 370 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.86(3H, t, $J=6.9$ Hz),
0.96(3H, t, $J=7.3$ Hz), 1.65(2H, m), 2.70–2.80(2H, m), 3.73–
3.81(2H, m), 5.63(1H, s), 7.31(1H, s), 7.42–7.44(2H, m),
7.72(1H, dd, $J=3.0, 6.4$ Hz), 9.65(1H, s), 12.08(1H, s).

10 IR(KBr): $\nu=3344, 3292, 2985, 2954, 2242, 1652$ cm $^{-1}$.

Example 181

Ethyl 4-(2,3-dibromophenyl)-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

A suspension of 2-bromo-3-nitrotoluene (5.0 g), iron
15 (3.9 g) and ammonium chloride (3.7 g) in ethanol (50 ml)-water
(17 ml) was heated under reflux for 2 hours. The insoluble
matter was filtered off. To the filtrate was added ethyl
acetate (100 ml) and the mixture was washed with water and a
saturated aqueous sodium chloride solution, and dried over
20 anhydrous magnesium sulfate. The solvent was evaporated and
the obtained residue was purified by silica gel column
chromatography (eluent: hexane-ethyl acetate (5:1)) to give a
pale-yellow oil (4.8 g). The obtained pale-yellow oil (4.8 g)
was dissolved in 47% hydrobromic acid (50 ml). Under ice-
25 cooling, an aqueous sodium nitrite (1.6 g) solution (18 ml)
was added and the mixture was stirred under ice-cooling for 30
minutes. The reaction mixture was added dropwise to a solution
of cuprous bromide (2.0 g) in 47% hydrobromic acid (20 ml)
over 30 minutes and the mixture was stirred at 60°C for 4.5
30 hours. To the reaction mixture was added water (100 ml) and
the mixture was extracted with ethyl acetate. The extract was
washed with water and a saturated aqueous sodium
hydrogencarbonate solution, and dried over anhydrous magnesium

sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (9:1)) to give 2,3-dibromotoluene (2.6 g) as a brown oil. A suspension of 2,3-dibromotoluene (2.6 g), N-bromosuccinimide (1.85 g) and benzoyl peroxide (50 mg) in carbon tetrachloride (30 ml) was heated under reflux for 2 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane) to give a colorless oil (1.1 g). To a solution of the obtained colorless oil (1.1 g) in dimethyl sulfoxide (8.6 ml) - methylene chloride (2 ml) was added trimethylamine-N-oxide (1.0 g) under ice-cooling and the mixture was stirred at room temperature for 1 hour. The reaction mixture was poured into water (50 ml) and the mixture was extracted with ethyl acetate. The extract was washed with 5% hydrochloric acid, a saturated aqueous sodium hydrogencarbonate solution and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give 2,3-dibromobenzaldehyde (0.5 g) as a brown oil. Then the title compound was prepared from 2,3-dibromobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:180-183°C (decomposition).

MS(EI):469(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.86(3H, t, J=7.3Hz), 0.96(3H, t, J=7.3Hz), 1.65(2H, m), 2.70-2.80(2H, m), 3.72-3.83(2H, m), 5.67(1H, s), 7.07(1H, d, J=5.8Hz), 7.18(1H, dd, J=5.8, 7.8Hz), 7.48(1H, d, J=7.8Hz), 9.57(1H, s), 12.02(1H, s).

IR(KBr):ν=3344, 3292, 2985, 2954, 2242, 1652cm⁻¹.

Example 182

Ethyl 4-(2-bromo-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate 1/2 H₂O

A suspension of 2-bromo-3-nitrotoluene (5.1 g), N-bromosuccinimide (4.2 g) and benzoyl peroxide (229 mg) in carbon tetrachloride (50 ml) was heated under reflux for 3 hours. The insoluble material was filtered off and the filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give a yellow solid (5.4 g). The obtained yellow solid (5.4 g) and hexamethylenetetramine (5.1 g) were dissolved in acetic acid-water (1:1, 16 ml) and the mixture was heated under reflux for 2 hours. To the reaction mixture was added concentrated hydrochloric acid (6 ml) and the mixture was heated under reflux for 15 minutes. The reaction mixture was extracted with ethyl acetate. The extract was washed with water, an aqueous sodium hydrogencarbonate solution and a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (5:1)) and crystallized (hexane-ethyl acetate (5:1)) to give 2-bromo-3-nitrobenzaldehyde (1.2 g) as yellow crystals. Subsequently, the title compound was prepared from 2-bromo-3-nitrobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP: 213-215°C.

Anal. Calcd. for: C₁₈H₁₉BrN₄O₄ 1/2 H₂O: C, 48.66; H, 4.54; N, 12.61.

Found: C, 48.34; H, 4.20; N, 13.04.

MS(EI): 435 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.3Hz), 0.97(3H, t, J=7.3Hz), 1.63-1.68(2H, m), 2.77-2.81(2H, m), 3.72-3.85(2H, m), 5.68(1H, s), 7.33-7.36(2H, m), 7.47(1H, dd, J=7.8, 7.8Hz), 7.66(1H, d, J=7.8Hz), 9.67(1H, s), 12.09(1H, s).

Example 183

Ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-bromo-m-xylene,
5 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner
as in Example 180.

MP:210-212°C (decomposition).

Anal. Calcd. for: C₁₉H₁₉BrN₄O₂: C, 54.95; H, 4.61; N, 13.49.

Found: C, 54.98; H, 4.94; N, 13.11.

10 MS(EI): 415(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=6.8Hz),
0.97(3H, t, J=7.3Hz), 1.62-1.68(2H, m), 2.75-2.80(2H, m), 3.72-
3.83(2H, m), 5.63(1H, s), 7.32(1H, s), 7.39-7.48(2H, m),
7.68(1H, dd, J=1.9, 7.3Hz), 9.65(1H, s), 12.07(1H, s).

15 **Example 184**

4-(2-Chloro-3-cyanophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
2-chloro-3-cyanobenzaldehyde and 3-aminopyrazole in the same
20 manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₇H₁₄Cl₃N₅: C, 63.06; H, 4.36; N, 21.63.

Found: C, 63.10; H, 4.42; N, 21.61.

MS(EI): 323(M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.61-
1.71(2H, m), 2.35-2.49(2H, m), 5.47(1H, s), 7.32(1H, s), 7.52-
7.59(2H, m), 7.87(1H, dd, J=2.0, 7.3Hz), 9.95(1H, s), 12.24(1H, s).

Example 185

4-(2-Chloro-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl butanoate,
2-chloro-3-nitrobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:234-235°C.

Anal. Calcd. for: C₁₆H₁₄ClN₅O₂: C, 55.90; H, 4.10; N, 20.37.

Found: C, 55.93; H, 4.34; N, 20.72.

MS(EI): 343(M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.64-
1.69(2H, m), 2.37-2.45(2H, m), 5.52(1H, s), 7.34(1H, s), 7.54-
7.60(2H, m), 7.89(1H, dd, J=2.0, 6.9Hz), 9.97(1H, s), 12.25(1H, s).

Example 186

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-
10 pyrazolo[3,4-b]pyridine 1/5 H₂O

The title compound was prepared from methyl butanoate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:275-279°C (decomposition).

15 Anal. Calcd. for: C₁₇H₁₄BrN₅ 1/5 H₂O: C, 55.05; H, 3.89; N, 18.88.

Found: C, 54.98; H, 3.91; N, 18.81.

MS(EI): 368(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.64-
1.69(2H, m), 2.38-2.43(2H, m), 5.47(1H, s), 7.33(1H, s), 7.54-
20 7.60(2H, m), 7.83(1H, dd, J=2.0, 7.4Hz), 9.95(1H, s), 12.24(1H, s).

Example 187

(+)-Ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-
propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of the compound (1.94 g) described in
25 Example 73 in acetonitrile (15 ml) was added (-)-10-
camphorsulfonic acid (1.23 g) at 50°C and the mixture was
stirred under ice-cooling for 30 minutes. The precipitated
crystals were collected by filtration and recrystallized
(ethanol-ethyl acetate (2:1), 30 ml) to give white crystals
30 (0.81 g). The obtained white crystals were suspended in water
and a saturated aqueous sodium hydrogencarbonate solution was
added. The mixture was extracted with ethyl acetate and the
extract was washed with water and a saturated aqueous sodium

chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated to give a colorless transparent oil. The obtained colorless transparent oil was crystallized from ethyl acetate to give the title compound (470 mg) as white
5 crystals.

MP:159-161°C.

Anal. Calcd. for: C₂₁H₂₅N₃O₃: C, 68.64; H, 6.86; N, 11.44.

Found: C, 68.37; H, 6.86; N, 11.26.

Specific rotation: [α]_D = +200° (EtOH, c=0.5).

10 MS(EI): 367(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.91(3H, t, J=6.8Hz),
0.98(3H, t, J=7.3Hz), 1.60-1.70(2H, m), 1.90-2.00(2H, m), 2.67-
2.82(4H, m), 3.81(2H, m), 4.25(2H, m), 5.42(1H, s),
6.62(1H, dd, J=7.4, 7.8Hz), 6.72-6.76(2H, m), 7.18(1H, s),
15 9.26(1H, s), 11.81(1H, s).

Example 188

(-)-Ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The filtrate obtained by filtering off the (-)-10-
20 camphorsulfonate salt in Example 187 was concentrated under reduced pressure and suspended in water. To the suspension was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution
25 and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was crystallized from ethyl acetate to give white crystals (780 mg). By the same process as in Example 187 using the obtained white crystals and (+)-10-camphorsulfonic acid, the title compound (150 mg)
30 was obtained as white crystals.

MP:160-161°C.

Anal. Calcd. for: C₂₁H₂₅N₃O₃: C, 68.64; H, 6.86; N, 11.44.

Found: C, 68.49; H, 6.81; N, 11.42.

Specific rotation: $[\alpha]_D = -202^\circ$ (EtOH, $c=0.5$)

MS(EI): 367 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, $J=6.8\text{Hz}$),
0.98(3H, t, $J=7.3\text{Hz}$), 1.60-1.70(2H, m), 1.90-2.00(2H, m), 2.67-
5 2.82(4H, m), 3.81(2H, m), 4.25(2H, m), 5.42(1H, s), 6.62(1H, dd,
 $J=7.4, 7.8\text{Hz}$), 6.72-6.76(2H, m), 7.18(1H, s), 9.26(1H, s),
11.81(1H, s).

Example 189

4-(2-Bromo-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-
10 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate,
2-bromo-3-nitrobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: 250-255°C (decomposition).

15 Anal. Calcd. for: $\text{C}_{16}\text{H}_{14}\text{BrN}_5\text{O}_2$: C, 49.50; H, 3.63; N, 18.04.

Found: C, 49.37; H, 3.76; N, 18.02.

MS(EI): 388 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, $J=7.6\text{Hz}$), 1.64-
1.70(2H, m), 2.39-2.44(2H, m), 5.53(1H, s), 7.34(1H, s),
20 7.49(1H, d, $J=7.8\text{Hz}$), 7.60(1H, dd, $J=7.8, 8.0\text{Hz}$),
7.82(1H, d, $J=8.0\text{Hz}$), 9.97(1H, s), 12.25(1H, s).

Example 190

Ethyl 4,7-dihydro-4-(2-methoxy-3-methylphenyl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

25 A suspension of 2,6-dimethylphenol (19.5 g), iodomethane
(31 ml) and potassium carbonate (33.2 g) in dimethylformamide
(200 ml) was stirred at 60°C for 10 hours. The reaction
mixture was poured into water (300 ml) and the mixture was
extracted with ethyl acetate. The extract was washed with a
30 saturated aqueous sodium chloride solution and dried over
anhydrous magnesium sulfate. The solvent was evaporated and
the obtained residue was purified by silica gel column
chromatography (eluent: hexane) to give 2-methoxy-m-xylene (12

g) as a colorless oil. A suspension of 2-methoxy-m-xylene (5.1 g), N-bromosuccinimide (4.2 g) and bezoyl peroxide (229 mg) in carbon tetrachloride (50 ml) was heated under reflux for 3 hours. The insoluble material was filtered off and the
5 filtrate was concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give a yellow solid (5.4 g). The obtained yellow solid (5.4 g) and hexamethylenetetramine (5.1 g) were dissolved in acetic acid-
10 water (1:1, 16 ml) and the mixture was heated under reflux for 2 hours. To the reaction mixture was added concentrated hydrochloric acid (6 ml) and the mixture was heated under reflux for 15 minutes. The reaction mixture was extracted with ethyl acetate. The extract was washed with water, an aqueous
15 sodium hydrogencarbonate solution and a saturated aqueous sodium chloride solution, and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (5:1)) and crystallized (hexane-ethyl
20 acetate (5:1)) to give 2-methoxy-3-methylbenzaldehyde (1.2 g) as yellow crystals. Subsequently, the title compound was prepared from 2-methoxy-3-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25. MP: 220-222°C.

25 Anal. Calcd. for: $C_{20}H_{25}N_3O_3$: C, 67.58; H, 7.09; N, 11.82.

Found: C, 67.47; H, 7.02; N, 11.91.

MS(EI): 355 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=7.0Hz),
0.97(3H, t, J=7.3Hz), 1.60-1.70(2H, m), 2.23(3H, s), 2.66-
30 2.85(2H, m), 3.81(3H, s), 3.81-3.85(2H, m), 5.43(1H, s), 6.82-
6.91(3H, m), 7.13(1H, s), 9.31(1H, s), 11.82(1H, s).

Example 191

Ethyl 4-(3-cyano-2-methoxyphenyl)-4,7-dihydro-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-methoxy-3-methylbenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 180.

5 MP:220-222°C.

Anal. Calcd. for: $C_{20}H_{22}N_4O_3$: C, 65.56; H, 6.05; N, 15.29.

Found: C, 65.20; H, 6.10; N, 15.23.

MS(EI): 366 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=7.1Hz),
10 0.96(3H, t, J=7.3Hz), 1.60-1.70(2H, m), 2.70-2.80(2H, m), 3.75-
3.90(2H, m), 4.02(3H, s), 5.46(1H, s), 7.14-7.19(2H, m),
7.32(1H, d, J=6.1Hz), 7.53(1H, d, J=7.8Hz), 9.51(1H, s),
11.97(1H, s).

Example 192

15 5-Cyano-6-ethyl-4,7-dihydro-4-(2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

20 MP:228-230°C (decomposition).

Anal. Calcd. for: $C_{15}H_{13}N_5O_2$: C, 61.01; H, 4.44; N, 23.72.

Found: C, 60.72; H, 4.51; N, 23.78.

MS(EI): 295 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.21(3H, t, J=7.4Hz), 2.42-
25 2.49(2H, m), 5.37(1H, s), 7.27(1H, s), 7.43-7.49(2H, m),
7.70(1H, dd, J=7.6, 8.0Hz), 7.89(1H, d, J=8.0Hz), 9.94(1H, s),
12.21(1H, s).

Example 193

5-Cyano-4-(2,3-dichlorophenyl)-6-ethyl-4,7-dihydro-2H-
30 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 2,3-dichlorobenzaldehyde, 3-aminopyrazole and 1-cyanobutan-2-one in the same manner as in Example 94.

MP:>300°C.

Anal. Calcd. for: C₁₅H₁₂Cl₂N₄: C, 56.44; H, 3.79; N, 17.55.

Found: C, 56.33; H, 3.86; N, 17.67.

MS(EI): 319(M⁺).

- 5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, t, J=7.6Hz), 2.38-2.49(2H, m), 5.43(1H, s), 7.23(1H, d, J=6.8Hz), 7.31-7.37(2H, m), 7.51(1H, dd, J=1.7, 8.1Hz), 9.92(1H, s), 12.19(1H, s).

Example 194

5-Cyano-6-ethyl-4,7-dihydro-4-(2-methoxyphenyl)-2H-

10 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 230-232°C.

- 15 Anal. Calcd. for: C₁₆H₁₆N₄O: C, 68.55; H, 5.75; N, 19.99.

Found: C, 68.16; H, 5.97; N, 20.39.

MS(EI): 280(M⁺).

- ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.22(3H, t, J=7.6Hz), 2.42-2.49(2H, m), 3.84(3H, s), 5.21(1H, s), 6.86-6.91(1H, m),
20 6.99(1H, d, J=8.3Hz), 7.05(1H, d, J=7.6Hz), 7.15-7.19(2H, m), 9.68(1H, s), 12.02(1H, s).

Example 195

4-(2-Chloro-3-cyanophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

- 25 The title compound was prepared from methyl propionate, 2-chloro-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>300°C.

Anal. Calcd. for: C₁₆H₁₂ClN₅: C, 62.04; H, 3.90; N, 22.61.

- 30 Found: C, 61.74; H, 4.14; N, 22.93.

MS(EI): 309(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, t, J=7.6Hz), 2.42-2.49(2H, m), 5.45(1H, s), 7.33(1H, s), 7.52-7.60(2H, m), 7.87

(1H,dd,J=2.0,7.3Hz), 9.97(1H,s), 12.23(1H,s).

Example 196

4-(2,1,3-Benzoxazol-4-yl)-5-cyano-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl propionate, 2,1,3-benzoxazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:206-208°C (decomposition).

Anal. Calcd. for: C₁₅H₁₂N₆O: C, 61.64; H, 4.14; N, 28.75.

10 Found: C, 61.43; H, 4.41; N, 28.85.

MS(EI): 292(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.20(3H,t,J=7.6Hz), 2.40-2.50(2H,m), 5.40(1H,s), 7.26(1H,s), 7.40(1H,d,J=6.6Hz), 7.58(1H,dd,J=6.6,9.0Hz), 7.92(1H,d,J=9.0Hz), 9.97(1H,s),

15 12.14(1H,s).

Example 197

4-(2-Chlorophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 20 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>300°C.

Anal. Calcd. for: C₁₅H₁₃ClN₄: C, 63.27; H, 4.60; N, 19.68.

Found: C, 63.14; H, 4.69; N, 19.67.

25 MS(EI): 284(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H,t,J=7.6Hz), 2.42-2.49(2H,m), 5.35(1H,s), 7.22-7.26(3H,m), 7.30-7.34(1H,m), 7.42(1H,d,J=7.8Hz), 9.85(1H,s), 12.15(1H,s).

Example 198

30 4-(2-Bromo-3-cyanophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same

manner as in Example 94.

MP:>300°C.

Anal. Calcd. for: C₁₆H₁₂BrN₅: C, 54.25; H, 3.41; N, 19.77.

Found: C, 54.13; H, 3.56; N, 19.98.

5 MS(EI): 354(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, t, J=7.6Hz), 2.43(2H, m),
5.46(1H, s), 7.33(1H, s), 7.56-7.60(2H, m), 7.82-7.84(1H, m),
9.98(1H, s), 12.24(1H, s).

Example 199

10 4-(2-Bromophenyl)-5-cyano-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

15 MP: 250-253°C (decomposition).

Anal. Calcd. for: C₁₅H₁₃BrN₄: C, 54.73; H, 3.98; N, 17.02.

Found: C, 54.28; H, 3.96; N, 16.94.

MS(EI): 329(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, t, J=7.6Hz), 2.42-
20 2.45(2H, m), 5.34(1H, s), 7.16(1H, dd, J=7.5, 7.6Hz),
7.22(1H, d, J=6.6Hz), 7.27(1H, s), 7.36(1H, dd, J=6.3, 7.3Hz),
7.59(1H, d, J=6.8Hz), 9.86(1H, s), 12.15(1H, s).

Example 200

Ethyl 4-(2-chlorophenyl)-6-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate 1/4 hydrate
25

A solution of 1,1'-carbonylbis-1H-imidazole (22.5 g), ethanol (8.1 ml) and toluene (100 ml) was stirred at room temperature for 1.5 hours. To the reaction mixture was added ice-water (100 ml) and the mixture was extracted with ethyl
30 acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent:

hexane-ethyl acetate (1:1)) to give a colorless oil (19.3 g). A solution of the obtained residue (19.3 g) and pyruvic aldehyde dimethyl acetal (11.1 ml) in toluene (50 ml) was added dropwise to a suspension of sodium hydride (8.44 g) in 5 toluene (250 ml) under reflux with heating over 15 minutes, and the mixture was heated under reflux for 1.5 hours. To the reaction mixture was added a 10% aqueous citric acid solution (610 ml) and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride 10 solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (5:1)) to give ethyl 4,4-dimethoxy-3-oxobutanoate (15.1 g) as a colorless oil. Subsequently, ethyl 4-(2- 15 chlorophenyl)-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate was obtained as a yellow solid from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 4,4-dimethoxy-2-oxobutanoate in the same manner as in Example 1. To a solution of ethyl 4-(2-chlorophenyl)-6-dimethoxymethyl-4,7- 20 dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (463 mg) in tetrahydrofuran (5 ml) was added 1N hydrochloric acid (10 ml) and the mixture was stirred at room temperature for 6 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with 25 ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give ethyl 4-(2-chlorophenyl)- 30 6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (290 mg) as a yellow solid. A solution of ethyl 4-(2-chlorophenyl)-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (290 mg) and hydroxylamine-O-sulfonic acid

(128.5 mg) in water (10 ml)-ethanol (10 ml) was stirred at 80°C for 2 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) and crystallized from ethanol-ethyl acetate to give the title compound (53 mg) as yellow crystals.

MP: 275-278°C (decomposition).

Anal. Calcd. for: $C_{16}H_{13}ClN_4O_2 \cdot \frac{1}{4} H_2O$: C, 57.66; H, 4.08; N, 16.81.

Found: C, 57.54; H, 4.06; N, 16.66.

MS(EI): 328 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.93(3H, t, J=7.1Hz), 3.91(2H, m), 5.67(1H, s), 7.15-7.19(2H, m), 7.25(1H, dd, J=7.3, 8.3Hz), 7.33(1H, s), 7.39(1H, d, J=8.3Hz), 10.81(1H, s), 12.34(1H, s).

Example 201

4-(2-Chloro-3-trifluoromethylphenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate, 2-chloro-3-trifluoromethylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: >250°C.

Anal. Calcd. for: $C_{17}H_{14}ClF_3N_4$: C, 55.67; H, 3.85; N, 15.28.

Found: C, 55.81; H, 3.97; N, 15.44.

MS(EI): 366 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, J=7.3Hz), 1.64-1.70(2H, m), 2.40-2.43(2H, m), 5.55(1H, s), 7.31(1H, s), 7.54-7.56(2H, m), 7.74(1H, dd, J=3.6, 5.6Hz), 9.93(1H, s), 12.22(1H, s).

Example 202

4-(2-Chloro-3-trifluoromethylphenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from benzoic acid, 2-chloro-3-trifluoromethylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:>250°C.

5 Anal. Calcd. for: C₂₀H₁₂ClF₃N₄: C, 59.94; H, 3.02; N, 13.98.

Found: C, 59.74; H, 3.18; N, 13.95.

MS(EI): 400(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.70(1H, s), 7.39(1H, s), 7.49-7.51(3H, m), 7.57-7.62(3H, m), 7.75-7.79(2H, m), 10.18(1H, s),
10 12.31(1H, s).

Example 203

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
15 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₆H₁₅ClN₄: C, 64.32; H, 5.06; N, 18.75.

Found: C, 64.18; H, 5.12; N, 18.84.

20 MS(EI): 298(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.23(3H, d, J=6.8Hz), 1.27(3H, d, J=6.8Hz), 3.06(1H, m), 5.34(1H, s), 7.22-7.26(3H, m), 7.30-7.34(1H, m), 7.42(1H, d, J=7.1Hz), 9.63(1H, s), 12.16(1H, s).

Example 204

25 Ethyl 1-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of the compound (1.2 g) described in Example 27 and dimethylaminopyridine (128 mg) in THF (40 ml) was added di-tert-butylidicarbonate (830 mg) and the mixture
30 was stirred at room temperature for one day. The solvent was evaporated under reduced pressure and the title compound (102 mg) was obtained as colorless crystals by silica gel column chromatography (eluent: hexane-ethyl acetate (3:1)).

MP:112-116°C.

Anal. Calcd. for: C₂₃H₂₈ClN₃O₄: C, 61.95; H, 6.33; N, 9.42.

Found: C, 61.84; H, 6.33; N, 9.34.

MS(EI): 445(M⁺).

5 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=6.9Hz),
0.98(3H, t, J=7.3Hz), 1.56(9H, s), 1.62-1.72(2H, m), 2.80-
2.92(2H, m), 3.85(2H, q, J=6.9Hz), 5.56(1H, s), 7.14-7.17(2H, m),
7.23(1H, dd, J=7.3 and 7.8Hz), 7.30(1H, s), 7.39(1H, d, J=7.4Hz),
8.75(1H, s).

10 **Example 205**

Ethyl 2-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography
used in Example 204 was further flowed hexane-ethyl acetate
15 (3:1) as an eluent, the title compound (300 mg) was obtained
as colorless crystals.

MP:144-147°C.

Anal. Calcd. for: C₂₃H₂₈ClN₃O₄: C, 61.95; H, 6.33; N, 9.42.

Found: C, 61.93; H, 6.35; N, 9.40.

20 MS(EI): 445(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.85(3H, t, J=6.9Hz),
0.97(3H, t, J=7.3Hz), 1.49(9H, s), 1.63-1.69(2H, m), 2.66-
2.85(2H, m), 3.80(2H, q, J=6.9Hz), 5.57(1H, s), 7.10-7.15(1H, m),
7.17(1H, ddd, J=1.5, 7.3 and 7.8Hz), 7.23(1H, dd, J=6.4 and 7.3Hz),
25 7.41(1H, d, J=7.2Hz), 7.67(1H, s), 10.01(1H, s).

Example 206

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-methoxycarbonyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous
30 solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and methyl chloroformate in the same manner as in Example 204.
MS(EI): 403(M⁺).

IR(KBr): ν =3422, 1736, 1699, 1531, 1450, 1232, 1086 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.87(3H, t, $J=7.1\text{Hz}$),
0.97(3H, t, $J=7.3\text{Hz}$), 1.60-1.66(2H, m), 2.86-2.89(2H, m),
3.83(2H, q, $J=7.1\text{Hz}$), 3.94(3H, s), 5.55(1H, s), 7.13-7.38(4H, m),
5 7.35(1H, s), 8.67(1H, s).

Example 207

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-methoxycarbonyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography
10 used in Example 206 was further flowed hexane-ethyl acetate
(3:1) as an eluent, the title compound was obtained as
colorless crystals.

MP:141-143°C.

MS(EI):403(M^+).

15 IR(KBr): ν =3290, 1774, 1695, 1633, 1597, 1523, 1444, 1364, 1307, 1209
 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.86(3H, t, $J=7.1\text{Hz}$),
0.95(3H, t, $J=7.3\text{Hz}$), 1.64-1.70(2H, m), 2.71-2.85(2H, m),
3.78(2H, q, $J=7.1\text{Hz}$), 3.85(1H, s), 5.57(1H, s), 7.10-7.24(3H, m),
20 7.42(1H, d, $J=1.4\text{Hz}$), 7.72(1H, s), 9.94(1H, s).

Example 208

Ethyl 1-benzyloxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals
25 from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-
pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine
and benzyl chloroformate in the same manner as in Example 204.

MP:80°C.

Anal. Calcd. for: $\text{C}_{26}\text{H}_{26}\text{ClN}_3\text{O}_4$: C, 65.07; H, 5.46; N, 8.75.

30 Found: C, 65.24; H, 5.71; N, 8.50.

MS(EI):479(M^+).

IR(KBr): ν =3344, 1745, 1701, 1527, 1451, 1226, 1084, 1060 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, $J=7.0\text{Hz}$),

0.94(3H,t,J=7.3Hz), 1.56-1.62(2H,m), 2.81-2.88(2H,m),
3.82(2H,q,J=7.0Hz), 5.41(2H,s), 5.55(1H,s), 7.13-7.24(3H,m),
7.36(1H,s), 7.37(6H,m), 8.62(1H,s).

Example 209

5 Ethyl 2-benzyloxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Further elution using the column of silica gel column chromatography in Example 208 and hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless
10 amorphous solid.

MS(EI):479(M⁺).

IR(KBr): ν =3294,1759,1697,1601,1383,1363,1300,1201 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.85(3H,t,J=7.0Hz),
0.95(3H,t,J=7.3Hz), 1.61-1.67(2H,m), 2.72-2.82(2H,m),
15 3.79(2H,q,J=7.0Hz), 5.30(2H,s), 5.56(1H,s), 7.09-7.41(9H,m),
7.73(1H,s), 9.95(1H,s).

Example 210

Ethyl 1-benzoyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and benzoyl chloride in the same manner as in Example 204.

MP:115°C.

25 Anal. Calcd. for:C₂₅H₂₄ClN₃O₃:C,66.74;H,5.38;N,9.34.

Found:C,66.58;H,5.41;N,9.28.

MS(EI):449(M⁺).

IR(KBr): ν =3414,1680,1641,1516,1095 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.90(3H,t,J=6.3Hz),
30 1.00(3H,t,J=7.3Hz), 1.65-1.71(2H,m), 2.90-2.93(2H,m),
3.85(2H,q,J=7.3Hz), 5.63(1H,s), 7.16-7.22(2H,m),
7.29(1H,d,J=7.3Hz), 7.40(1H,d,J=7.8Hz), 7.46(1H,s), 7.50-
7.54(2H,m), 7.65(1H,dd,J=6.3 and 7.8Hz), 7.98(1H,d,J=6.3Hz),

9.10(1H,s).

Example 211

Ethyl 2-benzoyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 Through the column of silica gel column chromatography used in Example 210 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MP:119-121°C.

10 Anal. Calcd. for: C₂₅H₂₄ClN₃O₃: C, 66.74; H, 5.38; N, 9.34.

Found: C, 66.58; H, 5.43; N, 9.30.

MS(EI): 479(M⁺).

IR(KBr): ν=3406, 1670, 1628, 1601, 1481, 1348, 1084 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=6.8Hz),

15 0.97(3H, t, J=7.3Hz), 1.65-1.67(2H, m), 2.74-2.83(2H, m),

3.82(2H, q, J=7.3Hz), 5.65(1H, s), 7.13-7.26(3H, m),

7.44(1H, d, J=7.8Hz), 7.47-7.51(2H, m), 7.60(1H, dd, J=7.3 and

7.3Hz), 7.91(2H, d, J=7.8), 8.00(1H, s), 10.06(1H, s).

Example 212

20 Ethyl 1-benzylcarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine
25 and phenylacetyl chloride in the same manner as in Example 204.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H, t, J=6.8Hz),

0.94(3H, t, J=7.3Hz), 1.60-1.61(2H, m), 2.84-2.86(2H, m),

3.82(2H, q, J=6.8Hz), 4.47(2H, s), 5.59(1H, s), 7.20-9.44(10H, m),

8.90(1H, s).

30 **Example 213**

Ethyl 2-benzylcarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography

used in Example 212 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MS(EI):463(M⁺).

5 IR(KBr): ν =3308,1699,1628,1630,1599,1523 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.87(3H,t,J=6.8Hz),
0.98(3H,t,J=7.3Hz), 1.65-1.71(2H,m), 2.77-2.84(2H,m),
3.83(2H,q,J=6.8Hz), 4.25(2H,s), 5.60(1H,s), 7.11-7.31(8H,m),
7.41(1H,d,J=7.8Hz), 7.84(1H,s), 10.30(1H,s).

10 **Example 214**

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-phenylcarbamoyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine
15 and phenyl isocyanate in the same manner as in Example 204.

MS(EI):464(M⁺).

IR(KBr): ν =3310,1699,1597,1518,1448,1369,1228,1194,1093 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.98(3H,t,J=7.1Hz),
20 0.97(3H,t,J=7.3Hz), 1.96(2H,m), 2.87(2H,m), 3.83(2H,q,J=7.1Hz),
5.61(1H,s), 7.11-7.69(8H,m), 7.67(2H,d,J=7.8Hz), 8.86(1H,s),
10.31(1H,s).

Example 215

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-phenylcarbamoyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 214 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as colorless crystals.

30 MP:145-147°C.

Anal. Calcd. for:C₂₅H₂₅ClN₄O₃:C,64.58;H,5.42;N,12.05.

Found:C,64.10;H,5.41;N,12.30.

MS(EI):464(M⁺).

IR(KBr): ν =3341, 1697, 1653, 1630, 1597, 1520, 1367, 1197, 1093 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, J =7.0Hz),
0.97(3H, t, J =7.3Hz), 1.68(2H, m), 2.80-2.92(2H, m),
3.82(2H, q, J =7.0Hz), 5.62(1H, s), 7.10-7.20(3H, m),
5 7.22(1H, dd, J =7.1 and 7.1Hz), 7.31-7.33(2H, m),
7.41(1H, d, J =7.1Hz), 7.58-7.60(2H, m), 7.85(1H, s), 9.67(1H, s),
9.83(1H, s).

Example 216

Ethyl 1-benzylcarbamoyl-4-(2-chlorophenyl)-4,7-dihydro-6-
10 propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and benzyl isocyanate in the same manner as in Example 204.

15 MS(EI): 478(M^+).

IR(KBr): ν =3402, 1699, 1637, 1525, 1226, 1091 cm^{-1} .

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, J =7.0Hz),
0.96(3H, t, J =7.3Hz), 1.61-1.63(2H, m), 2.83(2H, m),
3.82(2H, q, J =7.0Hz), 4.37(2H, d), 5.58(1H, s), 7.11-7.31(9H, m),
20 7.38(1H, d, J =7.8Hz), 8.74(1H, s), 9.01(1H, s).

Example 217

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-phenoxy-carbonyl-6-
propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous
25 solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and phenyl chloroformate in the same manner as in Example 204.

MS(EI): 465(M^+).

IR(KBr): ν =3339, 1728, 1633, 1525, 1371, 1302, 1224, 1091 cm^{-1} .

30 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.83(3H, t, J =7.1Hz),
0.96(3H, t, J =7.3Hz), 1.70(2H, m), 2.94(2H, m), 3.82(2H, q, J =7.1Hz),
5.62(1H, s), 7.12-7.53(9H, m), 8.26(1H, s), 9.30(1H, s).

Example 218

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-phenoxy-carbonyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 217 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as colorless crystals.

MP:156-157°C.

Anal. Calcd. for: $C_{25}H_{24}ClN_3O_4$: C, 64.44; H, 5.19; N, 9.02.

Found: C, 64.42; H, 5.31; N, 9.04.

10 MS(EI): 465 (M^+).

IR(KBr): $\nu=3325, 1765, 1685, 1597, 1525, 1373, 1205, 1099 \text{ cm}^{-1}$.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.87(3H, t, J=7.1Hz),
1.00(3H, t, J=7.3Hz), 1.67-1.69(2H, m), 2.76-2.85(2H, m),
3.82(2H, q, J=7.1Hz), 5.61(1H, s), 7.15(1H, dd, J=1.7 and 6.8Hz),
15 7.15(1H, dd, J=1.7 and 6.8Hz), 7.17(1H, dd, J=2.0 and 7.6Hz),
7.24(1H, dd, J=1.3 and 7.4Hz), 7.27-7.31(3H, m), 7.41-7.45(3H, m),
7.89(1H, s), 10.01(1H, s).

Example 219

Ethyl 4-(2-chlorophenyl)-1-ethoxycarbonyl-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and ethyl chloroformate in the same manner as in Example 204.

25 MP: 88-89°C.

Anal. Calcd. for: $C_{21}H_{24}ClN_3O_4$: C, 60.36; H, 5.79; N, 10.06.

Found: C, 60.24; H, 5.72; N, 10.05.

MS(EI): 417 (M^+).

IR(KBr): $\nu=3422, 1734, 1705, 1647, 1591, 1531, 1228, 1086, 1062 \text{ cm}^{-1}$.

30 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.87(3H, t, J=7.1Hz),
0.96(3H, t, J=7.3Hz), 1.31(3H, t, J=7.1Hz), 1.61-1.66(2H, m), 2.83-
2.92(2H, m), 3.83(2H, q, J=7.1Hz), 4.41(2H, q, J=7.1Hz), 5.55(1H, s),
7.13-7.16(2H, m), 7.25(1H, dd, J=7.0 and 7.6Hz), 7.34(1H, s),

7.38(1H,d,J=7.6Hz), 8.65(1H,s).

Example 220

Ethyl 4-(2-chlorophenyl)-2-ethoxycarbonyl-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

5 Through the column of silica gel column chromatography used in Example 219 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MS(EI):417(M⁺).

10 IR(KBr): ν =3325,1765,1685,1631,1597,1525,1373,1205,1099 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.87(3H,t,J=7.1Hz),
0.97(3H,t,J=7.3Hz), 1.26(3H,t,J=7.0Hz), 1.63-1.69(2H,m), 2.74-
2.81(2H,m), 3.81(2H,q,J=7.1Hz), 4.29(2H,q,J=7.0Hz), 5.57(1H,s),
7.12(1H,dd,J=6.3 and 7.5Hz), 7.17(1H,d,J=7.8Hz),
15 7.23(1H,dd,J=6.3 and 7.4Hz), 7.40(1H,d,J=7.8Hz), 7.71(1H,s),
9.96(1H,s).

Example 221

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-propoxycarbonyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

20 The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and propyl chloroformate in the same manner as in Example 204.
MP:66-68°C.

25 MS(EI):431(M⁺).

IR(KBr): ν =3356,1738,1695,1527,1282,1084 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.88(3H,t,J=7.0Hz),
0.92(3H,t,J=7.3Hz), 0.97(3H,t,J=7.3Hz), 1.62-1.67(2H,m), 1.70-
1.75(2H,m), 2.85-2.92(2H,m),3.83(2H,q,J=7.0Hz),
30 4.32(2H,t,J=6.5Hz), 5.57(1H,s), 7.14-7.18(2H,m),
7.26(1H,dd,J=6.3 and 7.6Hz), 7.35(1H,s), 7.39(1H,d,J=7.8Hz)
9.10(1H,s).

Example 222

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-propoxycarbonyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 221 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as colorless crystals.

MP:59°C.

Anal. Calcd. for: C₂₂H₂₆ClN₃O₄: C, 61.18; H, 6.07; N, 9.73.

Found: C, 60.81; H, 5.98; N, 9.74.

10 MS(EI): 431(M⁺).

IR(KBr): ν=3296, 1761, 1697, 1633, 1599, 1523, 1365, 1218, 1089 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.1Hz), 0.89(3H, t, J=7.5Hz), 0.97(3H, t, J=7.3Hz), 1.63-1.69(4H, m), 2.74-2.81(2H, m), 3.81(2H, q, J=7.1Hz), 4.21(2H, t, J=6.6Hz), 5.58(1H, s), 15 7.12(1H, dd, J=1.8 and 7.6Hz), 7.17(1H, ddd, J=1.9, 7.3 and 7.6Hz), 7.22(1H, ddd, J=1.2, 7.3 and 7.6Hz), 7.41(1H, dd, J=1.2 and 7.8Hz), 7.72(1H, s), 9.99(1H, s).

Example 223

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-isobutyryl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and isobutyryl chloride in the same manner as in Example 204.

25 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.0Hz), 0.96(3H, t, J=7.3Hz), 1.10(3H, d, J=6.9Hz), 1.14(3H, d, J=6.8Hz), 1.64-1.70(2H, m), 2.75-2.83(2H, m), 3.53(1H, q, J=7.0Hz), 3.83(2H, t, J=6.9Hz), 5.59(1H, s), 7.12(1H, s), 7.16(1H, dd, J=5.8 and 7.8Hz), 7.24(1H, dd, J=6.3 and 7.5Hz), 7.41(1H, s), 30 7.81(1H, s), 10.05(1H, s).

Example 224

Ethyl 1-acetyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and acetyl chloride in the same manner as in Example 204.

5 MP:75-76°C.

Anal. Calcd. for: C₂₀H₂₂ClN₃O₃: C, 61.93; H, 5.72; N, 10.83.

Found: C, 61.77; H, 5.78; N, 10.90.

MS(EI): 387(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H, t, J=7.3Hz),
10 0.97(3H, t, J=7.3Hz), 1.60-1.66(2H, m), 2.66(3H, s), 2.85-
2.90(2H, m), 3.81(2H, q, J=7.3Hz), 5.57(1H, s), 7.14-7.18(2H, m),
7.26(1H, dd, J=7.3 and 7.6Hz), 7.38(1H, s), 7.39(1H, d, J=8.1Hz),
8.90(1H, s).

Example 225

15 Ethyl 2-acetyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 224 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a
20 colorless amorphous solid.

MS(EI): 387(M⁺).

IR(KBr): ν=3306, 1699, 1633, 1601, 1523, 1371, 1197, 1086 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.0Hz),
0.96(3H, t, J=7.3Hz), 1.66(2H, m), 2.44(3H, s), 2.65-2.85(2H, m),
25 3.80(2H, q, J=7.0Hz), 5.58(1H, s), 7.09-7.22(3H, m),
7.40(1H, d, J=7.9Hz), 7.80(1H, s), 10.0(1H, s).

Example 226

Ethyl 1-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and butyl chloroformate in the same manner as in Example 204.

MS(EI):445(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.87(3H,t,J=7.3Hz),
0.88(3H,t,J=7.1Hz), 1.33-1.38(2H,m), 1.60-1.69(4H,m), 2.85-
2.87(2H,m), 3.82(2H,q,J=7.3Hz), 4.36(2H,t,J=6.5Hz), 5.55(1H,s),
5 7.13-7.17(2H,m), 7.25(1H,dd,J=6.4 and 6.5Hz), 7.34(1H,s),
7.37(1H,d,J=7.5Hz), 8.61(1H,s).

Example 227

Ethyl 2-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

10 Through the column of silica gel column chromatography used in Example 226 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless amorphous solid.

MS(EI):445(M⁺).

15 ¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.86(3H,t,J=7.3Hz),
0.87(3H,t,J=7.3Hz), 0.96(3H,t,J=7.3Hz), 1.31-1.32(2H,m),
1.61(4H,m), 2.73-2.80(2H,m), 3.80(2H,q,J=7.3Hz),
4.24(2H,t,J=6.5Hz), 5.57(1H,s), 7.09-7.22(3H,m),
7.39(1H,d,J=7.8Hz), 7.70(1H,s), 9.98(1H,s).

20 **Example 228**

Ethyl 4-(2-chlorophenyl)-1-cinnamoyl-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-
25 pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and cinnamoyl chloride in the same manner as in Example 204.

MP:131-134°C.

Anal. Calcd. for:C₂₇H₂₆ClN₃O₃:C,68.13;H,5.51;N,8.83.

Found:C,68.04;H,5.58;N,8.75.

30 MS(EI):475(M⁺).

IR(KBr):ν=3396,1687,1624,1521,1394,1207,1087 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.89(3H,t,J=7.0Hz),
0.98(3H,t,J=7.1Hz), 1.62-1.68(2H,m), 2.89-2.91(2H,m),

3.84(2H,q,J=7.0Hz), 5.60(1H,s), 7.16(1H,dd,J=7.4 and 7.8Hz),
7.18(1H,d,J=6.3Hz), 7.26(1H,dd,J=6.3 and 7.4Hz),
7.39(1H,d,J=7.8Hz), 7.45(1H,s), 7.46(3H,m), 7.67(1H,d,J=6.1Hz),
7.69-7.76(2H,m), 7.91(1H,d,J=7.4Hz), 9.01(1H,s).

5 **Example 229**

Ethyl 4-(2-chlorophenyl)-1-cinnamoyl-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

Through the column of silica gel column chromatography used in Example 228 was further flowed hexane-ethyl acetate
10 (3:1) as an eluent, the title compound was obtained as colorless crystals.

MS(EI):475(M⁺).

IR(KBr): ν =3304,1695,1674,1601,1521,1365,1168,1095 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.86(3H,t,J=7.0Hz),
15 0.98(3H,t,J=7.3Hz), 1.65-1.70(2H,m), 2.76-2.87(2H,m),
3.82(2H,q,J=7.0Hz), 5.62(1H,s), 7.12-7.18(2H,m),
7.24(1H,dd,J=7.3 and 7.3Hz), 7.42(1H,d,J=7.8Hz), 7.45-
7.46(3H,m), 7.60(1H,d,J=6.1Hz), 7.62-7.70(2H,m),
7.86(1H,d,J=6.1Hz), 7.85(1H,s), 10.09(1H,s).

20 **Example 230**

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-3-methyl-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 2-ethylbenzaldehyde, 3-amino-5-methylpyrazol and ethyl 3-
25 ketohexanoate in the same manner as in Example 25.

MP:164-165°C.

MS(EI):359(M⁺).

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.94(3H,t,J=7.0Hz),
1.02(3H,t,J=7.3Hz), 1.61(2H,m), 1.89(3H,s), 2.60-2.85(2H,m),
30 3.80(2H,q,J=7.0Hz), 5.44(1H,s), 7.00-7.30(4H,m), 9.39(1H,s),
11.66(1H,s).

Example 231

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-2-methyl-6-propyl-2H-

pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of ethyl 3-ketohexanoate (7.5 g), 2-chlorobenzaldehyde (6.6 g), piperidine (1.2 g) and acetic acid (2.25 g) in benzene (50 ml) was heated under reflux for 5 hours, and the reaction mixture was dehydrated using a Dean-Stark condenser. The solvent was evaporated under reduced pressure, and the residue was purified by silica gel column chromatography using an eluent (hexane-ethyl acetate (3:1)) to give ethyl 2-(2-chlorophenyl)methylen-3-oxohexanoate ((E)/(Z)=1:1 mixture) as a yellow oil. A solution of ethyl 2-(2-chlorophenyl)methylene-3-oxohexanoate ((E)/(Z)=1:1 mixture, 2.8 g), 3-amino-1-methylpyrazole (0.25 g) and p-toluenesulfonic acid (25 mg) in toluene (5 mL) and dimethylsulfoxide (0.5 mL) was heated under reflux for one day. The solvent was evaporated under reduced pressure, and the mixture was extracted with ethyl acetate (10 mL) and washed with a saturated aqueous sodium chloride solution. The organic layer was dried over anhydrous sodium sulfate and the solvent was evaporated under reduced pressure to give an oil. The obtained oil was purified by silica gel column chromatography (eluent (ethyl acetate-methanol (10:1))) to give the title compound as colorless crystals.

MP:150-151°C.

MS(EI):359(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.83(3H, t, J=7.0Hz), 0.96(3H, t, J=6.5Hz), 1.65(2H, m), 2.67-2.85(2H, m), 3.58(3H, s), 3.77(2H, q, J=7.0Hz), 5.55(1H, s), 7.07-7.11(2H, m), 7.19(1H, dd, J=7.4 and 7.8Hz), 7.24(1H, d, J=8.3Hz), 9.45(1H, s).

Example 232

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-1-methyl-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as a colorless amorphous solid from ethyl 2-(2-chlorophenyl)methylen-3-oxohexanoate

((E)/(Z)=1:1 mixture), 3-amino-2-methylpyrazole and p-toluenesulfonic acid.

MS(EI):359(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.84(3H, t, J=7.0Hz),
5 1.00(3H, t, J=7.1Hz), 1.67-1.69(2H, m), 2.70-2.88(2H, m),
3.65(3H, s), 3.80(2H, q, J=7.0Hz), 5.55(1H, s), 6.96(1H, s), 7.08-
7.12(2H, m), 7.20(1H, dd, J=6.8 and 7.8Hz), 7.35(1H, d, J=7.8Hz),
9.31(1H, s).

Example 233

10 Ethyl 4,7-dihydro-1-methyl-4-(naphthalen-1-yl)-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

A solution of ethyl 3-ketohexanoate (6.6 g), 1-naphthaldehyde (7.34 g), piperidine (1.2 g) and acetic acid (2.25 g) in benzene (50 mL) was heated under reflux for 3
15 hours and the reaction mixture was dehydrated using a Dean-Stark condenser. The solvent was evaporated and the residue was purified by silica gel column chromatography using an eluent (hexane-ethyl acetate (3:1)) to give ethyl 2-(naphthalen-1-yl)methylene-3-oxohexanoate ((E)/(Z)=1:1
20 mixture) as a yellow oil. The title compound was obtained as a colorless amorphous solid from ethyl 2-(naphthalen-1-yl)methylene-3-oxohexanoate ((E)/(Z)=1:1 mixture), 3-amino-2-methylpyrazole and p-toluenesulfonic acid.

MS(EI):375(M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.60(3H, t, J=6.9Hz),
1.03(3H, t, J=6.9Hz), 1.74(2H, m), 2.78-2.85(2H, m), 3.65(3H, s),
3.68(2H, q, J=6.9Hz), 5.94(1H, s), 6.76(1H, s), 7.20(1H, d, J=7.3Hz),
7.37(1H, dd, J=7.4 and 7.8Hz), 7.50(1H, dd, J=6.9 and 7.8Hz),
7.58(1H, m), 7.67(1H, d, J=8.3Hz), 7.88(1H, d, J=8.3Hz),
30 8.42(1H, d, J=8.8Hz), 9.26(1H, s).

Example 234

Ethyl 4-(3-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 3-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:140-143°C.

5 Anal. Calcd. for: $C_{18}H_{20}ClN_3O_2 \cdot 2/5 H_2O$: C, 61.24; H, 5.94; N, 11.90.

Found: C, 61.50; H, 5.94; N, 11.99.

MS(EI): 345 (M^+).

IR(KBr): ν =3263, 1736, 1666, 1591, 1514, 1275, 1222, 1207, 1087 cm^{-1} .

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, J=7.0Hz),

10 1.04(3H, t, J=7.1Hz), 1.58-1.63(2H, m), 2.63-2.81(2H, m),
3.86(2H, q, J=7.0Hz), 5.11(1H, s), 7.08(1H, d, J=7.8Hz), 7.12(2H, m),
7.21(1H, d, J=8.3Hz), 7.26(1H, s), 9.84(1H, s), 11.99(1H, s).

Example 235

Ethyl 4-(4-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-
15 b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 4-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:159-161°C.

20 Anal. Calcd. for: $C_{18}H_{20}ClN_3O_2 \cdot 1/5 H_2O$: C, 61.87; H, 5.88; N, 12.03.

Found: C, 61.92; H, 6.23; N, 11.95.

MS(EI): 345 (M^+).

IR(KBr): ν =3263, 1730, 1662, 1593, 1516, 1207, 1091 cm^{-1} .

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, J=7.0Hz),

25 0.95(3H, t, J=7.3Hz), 1.60(2H, m), 2.64-2.80(2H, m),
3.84(2H, q, J=7.0Hz), 5.10(1H, s), 7.13(2H, d, J=7.3Hz), 7.22(1H, s),
7.25(2H, d, J=7.3Hz), 9.45(1H, s), 11.96(1H, s).

Example 236

Ethyl 4,7-dihydro-4-(4-methyl-1H-imidazol-5-yl)-6-propyl-2H-
30 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 4-methyl-5-imidazolecarboxaldehyde, 3-aminopyrazole and ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:219-220°C.

Anal. Calcd. for: $C_{16}H_{21}N_5O_2 \cdot 1/2 H_2O$: C, 59.61; H, 6.25; N, 21.72.

Found: C, 59.34; H, 6.48; N, 22.06.

MS(EI): 315 (M^+).

5 IR(KBr): $\nu=3113, 2980, 1687, 1620, 1568, 1244, 1159 \text{ cm}^{-1}$.

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.94(3H, t, J=7.3Hz),
1.08(3H, t, J=7.0Hz), 1.58-1.59(2H, m), 2.21(3H, s), 2.58-
2.79(2H, m), 3.97(2H, q, J=7.3Hz), 5.50(1H, s), 6.14(1H, s),
7.14(1H, s), 7.19(1H, s), 9.78(1H, s), 11.53(1H, s).

10 **Example 237**

Ethyl 4,7-dihydro-4-(1-methyl-1H-imidazol-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 1-methyl-2-imidazolecarboxaldehyde, 3-aminopyrazole and
15 ethyl 3-ketohexanoate in the same manner as in Example 25.

MP:209°C.

Anal. Calcd. for: $C_{16}H_{21}N_5O_2 \cdot 3/5 H_2O$: C, 59.28; H, 6.28; N, 21.60.

Found: C, 59.00; H, 6.52; N, 21.55.

MS(EI): 315 (M^+).

20 IR(KBr): $\nu=3254, 3184, 3080, 1685, 1593, 1518, 1278, 1207, 1078 \text{ cm}^{-1}$.

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, J=6.8Hz),
0.93(3H, t, J=7.3Hz), 1.55-1.61(2H, m), 2.57-2.80(2H, m),
3.44(3H, s), 3.87(2H, q, J=6.8Hz), 5.29(1H, s), 6.56(1H, s),
6.84(1H, s), 7.27(1H, s), 9.38(1H, s), 11.97(1H, s).

25 **Example 238**

Ethyl 4,7-dihydro-4-(1H-imidazol-5-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from 3-imidazolecarboxaldehyde, 3-aminopyrazole and ethyl 3-
30 ketohexanoate in the same manner as in Example 25.

MP:200°C.

Anal. Calcd. for: $C_{15}H_{17}N_5O_2 \cdot 1/2 H_2O$: C, 58.43; H, 5.88; N, 22.71.

Found: C, 58.53; H, 6.25; N, 22.93.

MS(EI):301(M⁺).

IR(KBr): ν =3217,1655,1585,1506,1226,1205,1084 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.92(3H,t,J=7.3Hz),
1.01(3H,t,J=7.3Hz), 1.57-1.59(2H,m), 2.59-2.74(2H,m),
5 3.90(2H,q,J=7.3Hz), 5.12(1H,s), 6.35(1H,s), 7.35(1H,s),
7.38(1H,s), 9.21(1H,s), 11.91(1H,s).

Example 239

Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-butyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

10 The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-ketoheptanoate in the same manner as in Example 1.

MP:213°C.

Anal. Calcd. for:C₁₉H₂₁N₅O₃:C,62.11;H,5.76;N,19.06.

15 Found:C,62.08;H,5.75;N,18.95.

MS(EI):367(M⁺).

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.77(3H,t,J=7.3Hz),
0.92(3H,t,J=7.3Hz), 1.32-1.40(2H,m), 1.60-1.64(2H,m), 2.76-
2.86(2H,m), 3.76-3.82(2H,m), 5.68(1H,s), 7.11(1H,d,J=6.6Hz),
20 7.22(1H,s), 7.51(1H,dd,J=9.0Hz and 6.6Hz), 7.77(1H,d,J=9.0Hz),
9.65(1H,s), 12.00(1H,s).

Example 240

Ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-ethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

25 The title compound was prepared from 2,1,3-benzoxadiazole-4-aldehyde, 3-aminopyrazole and ethyl 3-ketopentanoate in the same manner as in Example 1.

MP:196°C.

Anal. Calcd. for:C₁₇H₁₇N₅O₃:C,60.17;H,5.05;N,20.64.

30 Found:C,60.09;H,5.15;N,20.41.

MS(EI):339(M⁺).

¹H-NMR (400MHz,DMSO-d₆) δ (ppm): 0.75 (3H,t, J=7.3Hz), 1.21 (3H,t, J=7.3Hz), 2.83(2H,q,J=7.3Hz), 3.73-3.84(2H,m), 5.68(1H,s),

7.12(1H,d,J=6.6Hz), 7.22(1H,s), 7.50(1H,dd,J=9.0Hz and 6.6Hz),
7.77(1H,d,J=9.0Hz), 9.68(1H,s), 12.01(1H,s).

Example 241

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-
5 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:174°C.

10 Anal. Calcd. for: C₁₇H₁₁ClN₄S 1/10 H₂O: C, 59.94; H, 3.31; N, 16.45.

Found: C, 59.82; H, 3.48; N, 16.93.

MS(EI): 338(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.50(1H,s), 7.18(1H,dd,J=7.3Hz
and 7.2Hz), 7.24-7.35(4H,m), 7.45(1H,d,J=7.8Hz),

15 7.60(1H,d,J=3.6Hz), 7.77(1H,d,J=3.9Hz), 10.08(1H,s),
12.29(1H,s).

Example 242

5-Cyano-4,7-dihydro-4-(2-methoxyphenyl)-6-(thiophen-2-yl)-2H-
pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl thiophene-2-carboxylate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:215°C.

Anal. Calcd. for: C₁₈H₁₄N₄OS: C, 64.65; H, 4.22; N, 16.75.

25 Found: C, 64.66; H, 4.32; N, 17.02.

MS(EI): 334(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.85(3H,s), 5.34(1H,s),
6.93(1H,dd,J=7.3Hz and 7.2Hz), 7.01(1H,d,J=7.3Hz), 7.14-
7.25(4H,m), 7.60(1H,d,J=3.6Hz), 7.77(1H,d,J=5.1Hz), 9.91(1H,s),
30 12.17(1H,s).

Example 243

5-Cyano-4,7-dihydro-4-(2-methylthiophenyl)-6-(thiophen-2-yl)-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2-methylthiobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:222°C.

5 Anal. Calcd. for: $C_{18}H_{14}N_4S_2 \cdot 2/5 H_2O$: C, 60.44; H, 4.17; N, 15.66.

Found: C, 60.58; H, 4.44; N, 15.35.

MS(EI): 350 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.49(3H, s), 5.48(1H, s), 7.17-7.28(5H, m), 7.33(1H, d, J=7.3Hz), 7.60(1H, d, J=3.7Hz),

10 7.77(1H, d, J=3.9Hz), 10.01(1H, s), 12.22(1H, s).

Example 244

5-Cyano-4,7-dihydro-4-(2-nitrophenyl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-
15 carboxylate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:165°C.

Anal. Calcd. for: $C_{17}H_{11}N_5O_2S$: C, 58.44; H, 3.17; N, 20.05.

Found: C, 58.15; H, 3.42; N, 20.38.

20 MS(EI): 349 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54(1H, s), 7.18(1H, dd, J=7.3Hz and 7.2Hz), 7.34(1H, s), 7.48-7.55(2H, m), 7.60(1H, d, J=3.7Hz), 7.72-7.79(2H, m), 7.92(1H, d, J=8.1Hz), 10.16(1H, s), 12.35(1H, s).

25 Example 245

4-(2,1,3-Benzothiadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2,1,3-benzothiadiazol-4-aldehyde and 3-
30 aminopyrazole in the same manner as in Example 95.

MP:254°C.

Anal. Calcd. for: $C_{17}H_{10}N_6S_2$: C, 56.34; H, 2.78; N, 23.19.

Found: C, 56.01; H, 2.91; N, 23.19.

MS(EI):362(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 5.84(1H, s), 7.19(1H, dd, J=4.4Hz and 4.3Hz), 7.28(1H, s), 7.55(1H, d, J=6.8Hz), 7.65(1H, d, J=3.7Hz), 7.72-7.79(2H, m), 7.99(1H, d, J=8.8Hz), 10.14(1H, s), 12.21(1H, s).

5 **Example 246**

5-Cyano-4,7-dihydro-4-(naphthalen-1-yl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, naphthalene-1-aldehyde and 3-aminopyrazole in the
10 same manner as in Example 95.

MP:214°C.

Anal. Calcd. for: C₂₁H₁₄N₄S: C, 71.16; H, 3.98; N, 15.81.

Found: C, 70.75; H, 3.96; N, 15.85.

MS(EI):354(M⁺).

15 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 5.87(1H, s), 7.13(1H, s),
7.18(1H, dd, J=4.6Hz and 3.9Hz), 7.45-7.54(4H, m),
7.62(1H, d, J=3.9Hz), 7.78(1H, d, J=4.9Hz), 7.83(1H, d, J=8.1Hz),
7.95(1H, d, J=9.3Hz), 8.31(1H, d, J=7.3Hz), 10.09(1H, s),
12.17(1H, s).

20 **Example 247**

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in
25 the same manner as in Example 95.

MP:232°C.

Anal. Calcd. for: C₁₇H₁₀Cl₂N₄S 1/10 H₂O: C, 54.44; H, 2.74; N, 14.94.

Found: C, 54.08; H, 2.90; N, 15.29.

MS(EI):373(M⁺).

30 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 5.58(1H, s), 7.18(1H, dd, J=7.3Hz and 7.2Hz), 7.32-7.41(3H, m), 7.54(1H, dd, J=7.3Hz and 1.5Hz),
7.60(1H, d, J=3.7Hz), 7.78(1H, d, J=4.9Hz), 10.14(1H, s),
12.32(1H, s).

Example 248**5-Cyano-4,7-dihydro-4-(2-methylphenyl)-6-phenyl-2H-pyrazolo[3,4-b]pyridine**

The title compound was prepared from methyl benzoate, 2-methylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:246°C.

Anal. Calcd. for: C₂₀H₁₆N₄ 1.0 H₂O: C, 72.71; H, 5.49; N, 16.96.

Found: C, 72.50; H, 5.26; N, 17.20.

10 MS(EI): 312(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.38(3H, s), 5.29(1H, s), 7.11-7.23(5H, m), 7.47-7.49(3H, m), 7.55-7.58(2H, m), 9.94(1H, s), 12.17(1H, s).

Example 249**5-Cyano-4,7-dihydro-4-(2-methylphenyl)-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine**

The title compound was prepared from methyl thiophene-2-carboxylate, 2-methylbenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

20 MP:276°C.

Anal. Calcd. for: C₁₈H₁₄N₄S: C, 67.90; H, 4.43; N, 17.60.

Found: C, 67.93; H, 4.54; N, 17.64.

MS(EI): 318(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.36(3H, s), 5.28(1H, s), 7.11-7.18(5H, m), 7.24(1H, s), 7.55(1H, dd, J=3.7Hz and 1.0Hz), 7.74(1H, dd, J=5.9Hz and 1.0Hz), 9.95(1H, s), 12.22(1H, s).

Example 250**4-(2-Chlorophenyl)-5-cyano-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine**

30 The title compound was prepared from methyl dimethoxyacetate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.39(6H, s), 5.18(1H, s),

5.43(1H,s), 7.23-7.27(3H,m), 7.32-7.35(1H,m),
7.44(1H,d,J=7.8Hz), 9.65(1H,s), 12.21(1H,s).

Example 251

4-(2-Chlorophenyl)-5-cyano-6-formyl-4,7-dihydro-2H-
5 pyrazolo[3,4-b]pyridine

4-(2-Chlorophenyl)-5-cyano-6-dimethoxymethyl-4,7-
dihydro-2H-pyrazolo[3,4-b]pyridine (4.4 g) was added to
trifluoroacetic acid (20 ml) under ice-cooling and the mixture
was stirred at room temperature for 2.5 hours. The reaction
10 mixture was concentrated under reduced pressure and
crystallized from ethyl acetate (50 ml) to give the title
compound (1.9 g) as yellow crystals.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 5.63(1H,s), 7.27-7.46(5H,m),
7.48(1H,d,J=7.1Hz), 9.73(1H,s), 10.17(1H,s), 12.34(1H,s).

15 Example 252

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-
pyrazolo[3,4-b]pyridine

To a suspension of 4-(2-chlorophenyl)-5-cyano-6-formyl-
4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (400 mg) in methanol
20 (10 ml) was added sodium borohydride (53 mg) under ice-cooling
and the mixture was stirred at the same temperature for 30
minutes. 10% Hydrochloric acid was added to the reaction
mixture, and a saturated sodium hydrogencarbonate solution was
added. The precipitated crystals were collected by filtration
25 and washed with ethanol to give the title compound (295 mg) as
yellow crystals.

MP:205-210°C (decomposition).

Anal. Calcd. for: C₁₄H₁₁ClN₄O 1/4 H₂O: C, 57.74; H, 3.98; N, 19.24.

Found: C, 57.38; H, 3.93; N, 18.94.

30 MS(EI): 286(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 4.29(2H,d,J=5.6Hz), 5.38(1H,s),
5.49(1H,t,J=5.6Hz), 7.22-7.34(4H,m), 7.43(1H,d,J=8.0Hz),
9.60(1H,s), 12.17(1H,s).

Example 253

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(trans-2-ethoxycarbonylethenyl)-2H-pyrazolo[3,4-b]pyridine

To a suspension of sodium hydride (94 mg) in
5 dimethoxyethane (10 ml) was added ethyl
diethylphosphonoacetate (528 mg) and the mixture was stirred
at room temperature for 15 minutes. Under ice-cooling, 4-(2-
chlorophenyl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-
b]pyridine (670 mg) was added to the mixture, and the mixture
10 was stirred at the same temperature for 1 hour. Water was
added to the reaction mixture and the mixture was extracted
with ethyl acetate. The extract was washed with a saturated
aqueous sodium chloride solution and dried over anhydrous
magnesium sulfate. The solvent was evaporated and the obtained
15 residue was purified by silica gel column chromatography
(eluent: hexane-ethyl acetate (1:1)) to give the title
compound (560 mg) as yellow crystals.

MP: 240-243°C (decomposition).

Anal. Calcd. for: $C_{18}H_{15}ClN_4O_2 \cdot \frac{1}{2} H_2O$: C, 59.43; H, 4.43; N, 15.40.

20 Found: C, 59.53; H, 4.26; N, 15.31.

MS(EI): 354 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.25(3H, d, J=7.1Hz),
4.21(2H, q, J=7.1Hz), 5.52(1H, s), 6.93(1H, d, J=15.9Hz), 7.27-
7.46(6H, m), 10.09(1H, s), 12.31(1H, s).

25 Example 254

4-(2-Chlorophenyl)-5-cyano-6-(2-ethoxycarbonylethyl)-4,7-
dihydro-2H-pyrazolo[3,4-b]pyridine

A suspension of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-
6-(trans-2-ethoxycarbonylethenyl)-2H-pyrazolo[3,4-b]pyridine
30 (260 mg) and 5% palladium on carbon (110 mg) in ethanol was
subjected to catalytic hydrogenation at room temperature for 5
hours. The reaction mixture was filtered through Celite and
the filtrate was concentrated under reduced pressure. The

obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give a yellow solid. The yellow solid was crystallized from ethyl acetate-diisopropyl ether to give the title compound (160 mg) as pale-yellow crystals.

MP: 172-174°C.

MS(EI): 356 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.18(3H, t, J=7.3Hz), 2.60-2.80(4H, m), 4.08(2H, q, J=7.3Hz), 5.35(1H, s), 7.20-7.31(4H, m), 7.42(1H, d, J=8.0Hz), 9.84(1H, s), 12.16(1H, s).

Example 255

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl dimethoxyacetate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.35(3H, s), 3.38(3H, s), 5.16(1H, s), 5.47(1H, s), 7.26(1H, s), 7.42(1H, d, J=6.6Hz), 7.60(1H, dd, J=6.6, 8.5Hz), 7.94(1H, d, J=8.5Hz), 9.77(1H, s), 12.19(1H, s).

Example 256

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 251.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.71(1H, s), 7.33(1H, s), 7.56(1H, d, J=6.6Hz), 7.62(1H, dd, J=6.6, 8.8Hz), 7.98(1H, d, J=8.8Hz), 9.73(1H, s), 10.32(1H, s), 12.32(1H, s).

Example 257

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-

benzoxadiazol-4-yl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 252. MP:215-220°C (decomposition).

Anal. Calcd. for: C₁₄H₁₀N₆O₂ 1/2 H₂O: C, 55.44; H, 3.66; N, 27.71.

5 Found: C, 55.32; H, 3.68; N, 27.31.

MS(EI): 294(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 4.30(2H, s), 5.45(1H, s),
5.52(1H, brs), 7.27(1H, s), 7.42(1H, d, J=6.6Hz),
7.59(1H, dd, J=6.6, 9.0Hz), 7.93(1H, d, J=9.0Hz), 9.71(1H, s),

10 12.16(1H, s).

Example 258

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(trans-2-ethoxycarbonylethenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 253.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.24(3H, d, J=7.1Hz),
4.21(2H, q, J=7.1Hz), 5.59(1H, s), 6.96(1H, d, J=16.1Hz),
7.32(1H, s), 7.39(1H, d, J=16.1Hz), 7.50(1H, m), 7.59(1H, m),
20 7.96(1H, d, J=8.3Hz), 10.21(1H, s), 12.29(1H, s).

Example 259

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(2-ethoxycarbonylethyl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(trans-2-ethoxycarbonylethenyl)-2H-pyrazolo[3,4-b]pyridine in the same manner as in Example 254.

MS(EI): 364(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.18(3H, t, J=7.1Hz), 2.66-
30 2.80(4H, m), 4.08(2H, q, J=7.1Hz), 5.40(1H, s), 7.26(1H, s),
7.42(1H, d, J=6.6Hz), 7.58(1H, dd, J=6.6, 9.0Hz),
7.92(1H, d, J=9.0Hz), 9.96(1H, s), 12.16(1H, s).

Example 260

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₇H₁₄BrN₅: C, 55.45; H, 3.83; N, 19.02.

Found: C, 55.30; H, 3.91; N, 18.98.

MS(EI): 368(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.23(3H, d, J=6.8Hz), 1.27(3H, d, J=6.8Hz), 3.03(1H, m), 5.45(1H, s), 7.33(1H, s), 7.55-7.82(2H, m), 7.83(1H, dd, J=2.0, 7.1Hz), 9.76(1H, s), 12.25(1H, s).

Example 261

4-(2-Bromophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine acetonitrile

The title compound was prepared from methyl isobutyrate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₆H₁₅BrN₄C₂H₃N: C, 56.26; H, 4.72; N, 18.22.

Found: C, 56.05; H, 4.56; N, 17.09.

MS(EI): 343(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.24(3H, d, J=7.1Hz), 1.27(3H, d, J=7.1Hz), 2.06(3H, s), 3.06(1H, m), 5.23(1H, s), 7.13-7.18(1H, m), 7.22(1H, d, J=7.6Hz), 7.27(1H, s), 7.36(1H, dd, J=1.2, 7.6Hz), 7.59(1H, dd, J=1.2, 8.0Hz), 9.64(1H, s), 12.17(1H, s).

Example 262

5-Cyano-4,7-dihydro-6-isopropyl-4-(2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:224°C.

MS(EI):309(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 1.23(3H,d,J=7.1Hz),
1.28(3H,d,J=7.1Hz), 3.03(1H,m), 5.36(1H,s), 7.27(1H,s), 7.43-
5 7.49(2H,m), 7.70(1H,dd,J=1.2,8.8Hz), 7.89(1H,dd,J=1.2,8.3Hz),
9.71(1H,s), 12.23(1H,s).

Example 263

5-Cyano-4-(2,3-dichlorophenyl)-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl isobutyrate,
2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:>250°C.

Anal. Calcd. for:C₁₆H₁₄Cl₂N₄:C,57.67;H,4.23;N,16.89.

15 Found:C,57.74;H,4.27;N,16.89.

MS(EI):333(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 1.23(3H,d,J=7.1Hz),
1.27(3H,d,J=7.1Hz), 3.04(1H,m), 5.42(1H,s), 7.23(1H,d,J=7.6Hz),
7.31(1H,s), 7.35(1H,dd,J=7.6,7.8Hz), 7.51(1H,dd,J=1.5,7.8Hz),
20 9.70(1H,s), 12.21(1H,s).

Example 264

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
25 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the
same manner as in Example 94.

MP:222-223°C (decomposition).

Anal. Calcd. for:C₁₆H₁₄N₆O:C,62.71;H,4.61;N,27.44.

Found:C,62.71;H,4.65;N,27.45.

30 MS(EI):306(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 1.24(3H,d,J=7.1Hz),
1.25(3H,d,J=7.1Hz), 3.03(1H,m), 5.39(1H,s), 7.26(1H,s),
7.40(1H,d,J=6.6Hz), 7.58(1H,dd,J=6.6,8.8Hz),

7.92(1H,d,J=8.8Hz), 9.74(1H,s), 12.15(1H,s).

Example 265

5-Cyano-4,7-dihydro-6-isopropyl-4-(2-methoxyphenyl)-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl isobutyrate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₇H₁₈N₄O: C, 69.37; H, 6.16; N, 19.03.

10 Found: C, 69.13; H, 6.21; N, 19.54.

MS(EI): 294(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.23(3H,d,J=7.1Hz),
1.28(3H,d,J=7.1Hz), 3.09(1H,m), 3.83(3H,s), 5.19(1H,s),
6.90(1H,dd,J=7.4,7.6Hz), 6.99(1H,d,J=7.6Hz),
15 7.05(1H,dd,J=1.7,7.4Hz), 7.15-7.19(2H,m), 9.47(1H,s),
12.04(1H,s).

Example 266

4-(2-Chlorophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl cyclopropanecarboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₆H₁₃ClN₄: C, 64.76; H, 4.42; N, 18.88.

25 Found: C, 64.71; H, 4.50; N, 19.05.

MS(EI): 296(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89-0.93(2H,m), 1.00-1.15(2H,m),
2.01(1H,m), 5.35(1H,s), 7.22-7.26(3H,m), 7.31-7.34(1H,m),
7.42(1H,d,J=7.8Hz), 9.14(1H,s), 12.16(1H,s).

30 **Example 267**

4-(2-Bromophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl

cyclopropanecarboxylate, 2-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₆H₁₃BrN₄: C, 56.32; H, 3.84; N, 16.42.

5 Found: C, 56.18; H, 3.90; N, 16.48.

MS(EI): 341(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-0.93(2H, m), 1.00-1.15(2H, m), 2.01(1H, m), 5.34(1H, s), 7.13-7.22(2H, m), 7.27(1H, s), 7.34-7.38(1H, m), 7.59(1H, d, J=6.8Hz), 9.15(1H, s), 12.16(1H, s).

10 **Example 268**

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine 1/4 acetonitrile

The title compound was prepared from methyl cyclopropanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:>250°C.

Anal. Calcd. for: C₁₇H₁₂BrN₅H₂O 1/4 CH₃CN: C, 53.28; H, 3.77; N, 18.64.

Found.: C, 53.28; H, 3.72; N, 18.81.

MS(EI): 366(M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-0.93(2H, m), 1.03-1.08(2H, m), 1.96-2.00(1H, m), 5.45(1H, s), 7.32(1H, s), 7.54-7.60(2H, m), 7.83(1H, dd, J=1.7, 7.1Hz), 9.27(1H, s), 12.25(1H, s).

Example 269

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopropanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 200-201°C (decomposition).

30 Anal. Calcd. for: C₁₆H₁₂N₆O H₂O: C, 59.62; H, 4.38; N, 26.07.

Found: C, 59.93; H, 4.05; N, 26.19.

MS(EI): 304(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88-0.93(2H, m), 1.01-1.12(2H, m),

1.99(1H,m), 5.39(1H,s), 7.25(1H,s), 7.40(1H,d,J=6.6Hz),
7.59(1H,dd,J=6.6,9.0Hz), 7.92(1H,d,J=9.0Hz), 9.26(1H,s),
12.15(1H,s).

Example 270

5 4-(2-Methoxyphenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine 1/4 acetonitrile

The title compound was prepared from methyl cyclopropanecarboxylate, 2-methoxybenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

10 MP:241-243°C.

Anal. Calcd. for: C₁₇H₁₆N₄O 1/4 CH₃CN: C, 69.46; H, 5.58; N, 19.67.

Found: C, 69.35; H, 5.56; N, 19.64.

MS(EI): 292(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-0.92(2H,m), 0.99-1.10(2H,m),
15 2.01-2.06(1H,m), 3.84(3H,s), 5.21(1H,s),
6.90(1H,dd,J=7.3,7.6Hz), 6.98-7.05(2H,m), 7.15-7.19(2H,m),
8.97(1H,s), 12.04(1H,s).

Example 271

20 5-Cyano-6-cyclopropyl-4-(2,3-dichlorophenyl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine 1/4 acetonitrile

The title compound was prepared from methyl cyclopropanecarboxylate, 2,3-dichlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: >250°C.

25 Anal. Calcd. for: C₁₆H₁₂Cl₂N₄ 1/4 CH₃CN: C, 58.04; H, 3.76; N, 17.43.

Found: C, 57.87; H, 3.79; N, 17.44.

MS(EI): 331(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-0.93(2H,m), 1.03-1.08(2H,m),
1.98-2.03(1H,m), 5.43(1H,s), 7.22(1H,d,J=7.8Hz), 7.31(1H,s),
30 7.35(1H,t,J=7.8Hz), 7.51(1H,dd,J=1.5,7.8Hz), 9.21(1H,s),
12.20(1H,s).

Example 272

5-Cyano-6-cyclopropyl-4,7-dihydro-4-(2-nitrophenyl)-2H-

pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopropanecarboxylate, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

5 MP:236-238°C (decomposition).

Anal. Calcd. for: C₁₆H₁₃N₅O₂: C, 62.53; H, 4.26; N, 22.79.

Found: C, 62.54; H, 4.29; N, 22.85.

MS(EI): 307(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-0.93(2H, m), 1.01-1.09(2H, m),
10 1.99(1H, m), 5.37(1H, s), 7.27(1H, s), 7.42-7.49(2H, m),
7.70(1H, dd, J=7.5, 7.6Hz), 7.90(1H, d, J=8.1Hz), 9.23(1H, s),
12.22(1H, s).

Example 273

Ethyl 4-(2-chlorophenyl)-6-dimethoxymethyl-4,7-dihydro-2H-
15 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 4,4-dimethoxy-3-oxobutanoate in the same manner as in Example 1.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.87(3H, t, J=7.1Hz), 3.35(3H, s),
20 3.46(3H, s), 3.82(2H, m), 5.64(1H, s), 6.11(1H, s), 7.10-7.14(2H, m),
7.20-7.24(1H, m), 7.27(1H, s), 7.36(1H, d, J=8.3Hz), 8.94(1H, s),
12.05(1H, s).

Example 274

Ethyl 4-(2-chlorophenyl)-6-formyl-4,7-dihydro-2H-pyrazolo[3,4-
25 b]pyridine-5-carboxylate

To a solution of ethyl 4-(2-chlorophenyl)-6-dimethoxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine-5-carboxylate (463 mg) in tetrahydrofuran (5 ml) was added 1N hydrochloric acid (10 ml) and the mixture was stirred at room
30 temperature for 6 hours. To the reaction mixture was added a saturated aqueous sodium hydrogencarbonate solution and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and

dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give the title compound (290 mg) as a yellow solid.

5 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=7.3Hz), 3.91(2H, m), 5.70(1H, s), 7.14-7.24(3H, m), 7.31(1H, s), 7.40(1H, d, J=7.8Hz), 9.64(1H, s), 10.23(1H, s), 12.19(1H, s).

Example 275

Ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

2-Chlorobenzaldehyde (1.41 g), 3-aminopyrazole (0.83 g) and ethyl isobutyrylacetate (1.58 g) were stirred in acetic acid (10 ml) at 80°C for 2 hours. Under ice-cooling, a saturated aqueous sodium hydrogencarbonate solution was added
15 to the reaction mixture. The insoluble material was filtered off, and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The extract was concentrated under reduced pressure and the
20 obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)). The purified product was crystallized from hexane-ethyl acetate to give the title compound (115 mg) as white crystals.

MP: 211-213°C.

25 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.85(3H, t, J=7.1Hz), 1.16(3H, m), 1.28(3H, d, J=7.1Hz), 3.76(2H, m), 4.35(1H, m), 5.59(1H, s), 7.07-7.13(2H, m), 7.18-7.22(1H, m), 7.24(1H, s), 7.35(1H, dd, J=1.2, 8.1Hz), 9.14(1H, s), 11.97(1H, s).

Example 276

30 Ethyl 4-(2-bromophenyl)-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from 2-bromobenzaldehyde, 3-aminopyrazole and ethyl isobutyrylacetate in the same manner

as in Example 275.

MP: 214–215°C.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=6.8Hz), 1.16(3H, m),
1.28(3H, d, J=6.8Hz), 3.76(2H, m), 4.35(1H, m), 5.56(1H, s), 7.07–
5 7.13(2H, m), 7.02(1H, dd, J=7.3, 7.8Hz), 7.11(1H, d, J=6.4Hz),
7.24(1H, dd, J=7.4, 7.8Hz), 7.28(1H, s), 7.52(1H, d, J=7.8Hz),
9.15(1H, s), 11.98(1H, s).

Example 277

Ethyl 4-(2-chlorophenyl)-6-cyclopropyl-4,7-dihydro-2H-
10 pyrazolo[3,4-b]pyridine-5-carboxylate

To a solution of 2-oxazolydone (20.8 g) in tetrahydrofuran (750 ml) was added n-butyllithium (1.56 M hexane solution, 153 ml) at -78°C and the mixture was stirred at the same temperature for 30 minutes. To the reaction
15 mixture was added a solution of cyclopropanecarbonyl chloride (25 g) in tetrahydrofuran (50 ml) at -78°C over 30 minutes. The mixture was stirred for 14 hours while gradually raising the temperature to room temperature. The reaction mixture was poured into ice-water and the mixture was extracted with ethyl
20 acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The extract was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give
25 white crystals (26 g). A mixture of the obtained white crystals (10 g), ethyl bromoacetate (21.5 ml) and zinc powder (25.3 g) in tetrahydrofuran (300 ml) was ultrasonicated for 2 hours and heated under reflux for 2 hours. To the reaction mixture was added 10% hydrochloric acid and the insoluble
30 material was filtered off through Celite. The filtrate was extracted with ethyl acetate, and the extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The extract was concentrated

under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give ethyl 3-cyclopropyl-3-oxopropionate (5.7 g) as a yellow oil. Subsequently, the title compound was
5 prepared from 2-chlorobenzaldehyde, 3-aminopyrazole and ethyl 3-cyclopropyl-3-oxopropionate in the same manner as in Example 275.

MP:190-192°C.

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.83-0.93(4H,m), 1.10(1H,m),
10 3.14(1H,m), 3.80(2H,m), 5.60(1H,s), 7.08-7.12(2H,m), 7.18-
7.22(1H,m), 7.25(1H,s), 7.34(1H,d,J=8.3Hz), 8.62(1H,s),
11.99(1H,s).

Example 278

4-(2-Bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine
15

The title compound was prepared from methyl thiophene-2-carboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:>280°C.

20 Anal. Calcd. for: C₁₈H₁₀BrN₅S: C, 52.95; H, 2.47; N, 17.15.

Found: C, 52.72; H, 2.69; N, 17.21.

MS(EI): 408(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 5.62(1H,s), 7.18(1H,dd,J=5.1Hz and 3.7Hz), 7.40(1H,s), 7.59-7.67(3H,m), 7.79(1H,d,J=3.9Hz),
25 7.86(1H,dd,J=7.6Hz and 2.0Hz), 10.20(1H,s), 12.37(1H,s).

Example 279

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-methyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate 2-chlorobenzaldehyde and 3-amino-5-methylpyrazole in the same
30 manner as in Example 94.

MP:260°C.

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.91(3H,t,J=7.3Hz), 1.60-

1.65(2H,m), 1.71(3H,s), 2.33(2H,q,J=7.3Hz), 5.27(1H,s), 7.20-7.24(2H,m), 7.31(1H,dd,J=7.3Hz and 7.2Hz), 7.39(1H,d,J=7.3Hz), 9.68(1H,s), 11.83(1H,s).

Example 280

5 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-phenyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butanoate 2-chlorobenzaldehyde and 3-amino-5-phenylpyrazole in the same manner as in Example 94.

10 MP:262°C.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.89(3H,t,J=7.3Hz), 1.61-1.63(2H,m), 2.36(2H,q,J=7.3Hz), 5.61(1H,s), 7.09-7.34(9H,m), 9.89(1H,s), 12.62(1H,s).

Example 281

15 1-tert-Butoxycarbonyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine

The title compound was obtained as a colorless amorphous solid from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and di-tert-
20 butyl dicarbonate in the same manner as in Example 204.

MP:98-102°C.

MS(EI):398(M⁺).

IR(KBr):ν=3391,2199,1723,1643,1529,1394,1149 cm⁻¹.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.95(3H,t,J=7.3Hz), 1.57(3H,s),
25 1.60-1.67(2H,m), 2.53-2.61(2H,m), 5.38(1H,s), 7.25-7.31(3H,m), 7.35(1H,ddd,J=1.4,7.3 and 7.8Hz), 7.45(1H,d,J=8.1Hz), 9.20(1H,s).

Example 282

30 2-tert-Butoxycarbonyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

Through the column of silica gel column chromatography used in Example 281 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as

colorless crystals.

MP:175°C (decomposition).

Anal. Calcd. for: C₂₁H₂₃ClN₄O₂: C, 63.23; H, 5.81; N, 14.05.

Found: C, 62.91; H, 5.80; N, 13.82.

5 MS(EI): 398(M⁺).

IR(KBr): ν=3329, 2197, 1747, 1612, 1523, 1369, 1311, 1151, 949 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.93(3H, t, J=7.4Hz),
1.65(2H, q, J=7.3Hz), 2.40-2.44(2H, m), 2.48(9H, s), 5.32(1H, s),
7.27-7.36(3H, m), 7.45(1H, d, J=7.8Hz), 7.68(1H, s), 10.32(1H, s).

10 **Example 283**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-1-phenylcarbamoyl-6-propyl-1H-pyrazolo[3,4-b]pyridine

The title compound was obtained as a colorless amorphous solid from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and phenyl isocyanate in the same manner as in Example 204.

MP:138-140°C.

Anal. Calcd. for: C₂₃H₂₀ClN₅O 1/4 H₂O: C, 65.4; H, 4.89; N, 16.58.

Found: C, 65.20; H, 5.05; N, 16.17

20 MS(EI): 417(M⁺).

IR(KBr): ν=3387, 3294, 2202, 1712, 1537 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.95(3H, t, J=7.3Hz),
1.63(2H, q, J=7.4Hz), 2.58(2H, m), 5.43(1H, s), 7.13(1H, dd, J=7.4
and 7.5Hz), 7.24-7.36(6H, m), 7.46(1H, d, J=7.8Hz),
25 7.69(2H, d, J=7.8Hz), 9.46(1H, s), 10.38(1H, s).

Example 284

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-2-phenylcarbamoyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

Through the column of silica gel column chromatography used in Example 283 was further flowed hexane-ethyl acetate (3:1) as an eluent, the title compound was obtained as a colorless oil.

MP:167-171°C.

MS(EI): 417(M⁺).

IR(KBr): ν =3215, 2204, 1732, 1631, 1523, 1375 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.97(3H, t, J=7.4Hz),
1.65(2H, q, J=7.3Hz), 2.48(2H, m), 5.39(1H, s), 6.95(1H, dd, J=7.3
5 and 7.3Hz), 7.11(2H, dd, J=7.3 and 7.6Hz), 7.24-7.49(4H, m),
7.61(2H, d, J=7.8Hz), 7.88(1H, s), 8.63(1H, s), 9.77(1H, s),
10.17(1H, s).

Example 285

2-Acetoxyacetyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-
10 propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine, dimethylaminopyridine and
acetoxyacetyl chloride in the same manner as in Example 204.

15 MP: 149-150°C.

Anal. Calcd. for: C₂₀H₁₉ClN₄O₃: C, 60.23; H, 4.80; N, 14.05.

Found: C, 60.17; H, 4.83; N, 13.90.

MS(EI): 398(M⁺).

IR(KBr): ν =3281, 3238, 2197, 1745, 1630, 1608, 1523, 1385, 1344, 1236,
20 1172 cm⁻¹.

¹H-NMR (400MHz, DMSO-d₆) δ (ppm): 0.95(3H, t, J=7.3Hz), 1.64-
1.70(2H, m), 2.44(2H, q, J=7.3Hz), 3.33(3H, s), 5.26(2H, s),
5.37(1H, s), 7.29-7.35(3H, m), 7.46(1H, d, J=7.8Hz), 7.86(1H, s),
10.45(1H, s).

25 **Example 286**

Ethyl 1-acetoxyacetyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-
1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals
from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-
30 pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine
and acetoxyacetyl chloride in the same manner as in Example
204.

MP: 130-131°C.

Anal. Calcd. for: $C_{22}H_{24}ClN_3O_5$: C, 59.26; H, 5.43; N, 9.42.

Found: C, 59.17; H, 5.39; N, 9.31.

MS(EI): 445 (M^+).

IR(KBr): $\nu=3337, 1732, 1529, 1390, 1246, 1086 \text{ cm}^{-1}$.

5 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, $J=7.0\text{Hz}$),
0.97(3H, t, $J=7.3\text{Hz}$), 1.64-1.70(2H, m), 2.76-2.82(2H, m),
3.31(3H, s), 3.85(2H, q, $J=7.0\text{Hz}$), 5.27(2H, dd, $J=3.0$ and 9.8Hz),
5.60(1H, s), 7.10-7.25(3H, m), 7.41(1H, dd, $J=1.4$ and 8.0Hz),
7.82(1H, s), 10.1(1H, s).

10 **Example 287**

Ethyl 1-benzylcarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was obtained as colorless crystals from ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate, dimethylaminopyridine and phenylacetyl chloride in the same manner as in Example 204.

MS(EI): 463 (M^+).

IR(KBr): $\nu=3418, 1701, 1521, 1392, 1228 \text{ cm}^{-1}$.

15 $^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, $J=7.0\text{Hz}$),
0.93(3H, t, $J=7.3\text{Hz}$), 1.57-1.62(2H, m), 2.80-2.87(2H, m),
3.82(2H, q, $J=7.0\text{Hz}$), 4.33(2H, s), 5.57(1H, s), 7.15(1H, dd, $J=7.4$
and 7.8Hz), 7.18-7.31(7H, m), 7.39(1H, d, $J=7.8\text{Hz}$), 7.44(1H, s),
8.94(1H, s).

Example 288

25 4-(2,1,3-Benzoxadiazol-4-yl)-2-tert-butoxycarbonyl-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and tert-butylidicarbonate in the same manner as in Example 204.

MP: 168-170°C.

Anal. Calcd. for: $C_{21}H_{22}N_6O_3$: C, 62.06; H, 5.46; N, 20.68.

Found: C, 61.92; H, 5.44; N, 20.52.

MS(EI):406(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.89(3H,t,J=7.3Hz), 1.47(9H,s),
1.65(2H,m), 2.40(2H,m), 5.39(1H,s), 7.49(1H,d,J=6.3Hz),
7.60(1H,dd,J=6.6 and 9.0Hz), 7.79(1H,s), 7.96(1H,d,J=6.6Hz),
5 10.43(1H,s).

Example 289

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-1-phenylcarbamoyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
10 from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and phenyl isocyanate in the same manner as in Example 204.

MP:138-140°C.

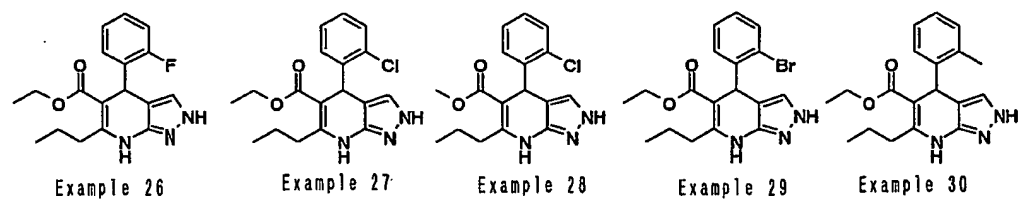
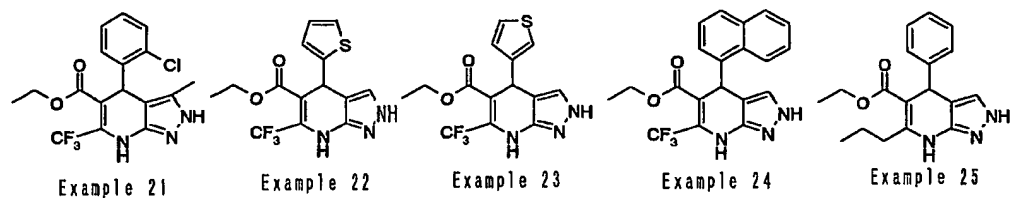
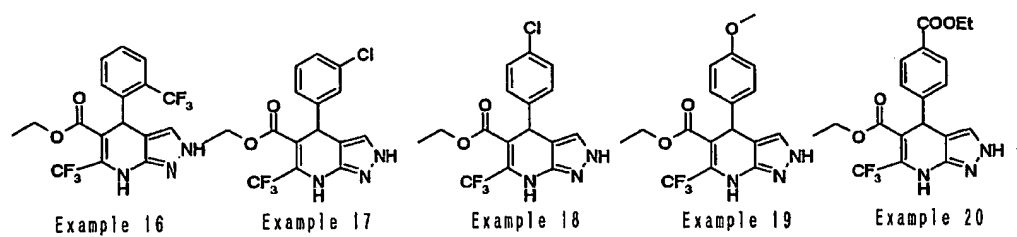
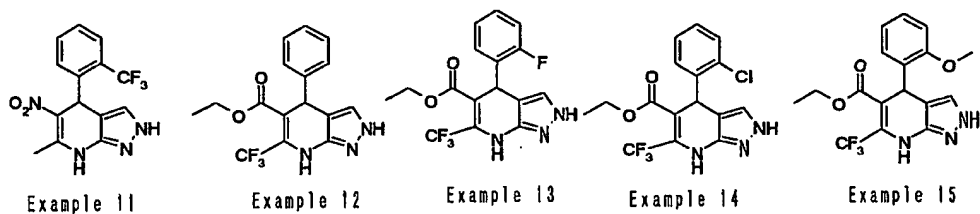
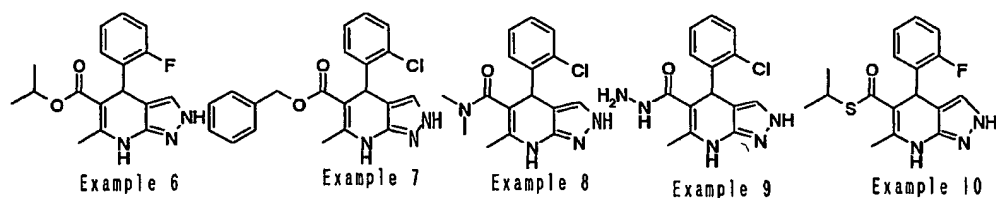
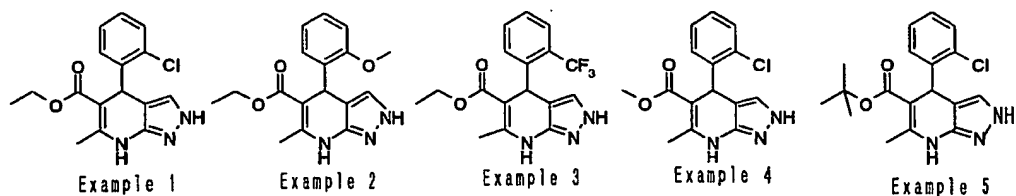
Anal. Calcd. for:C₂₃H₁₉N₇O₂:C,64.93;H,4.50; N,23.05.

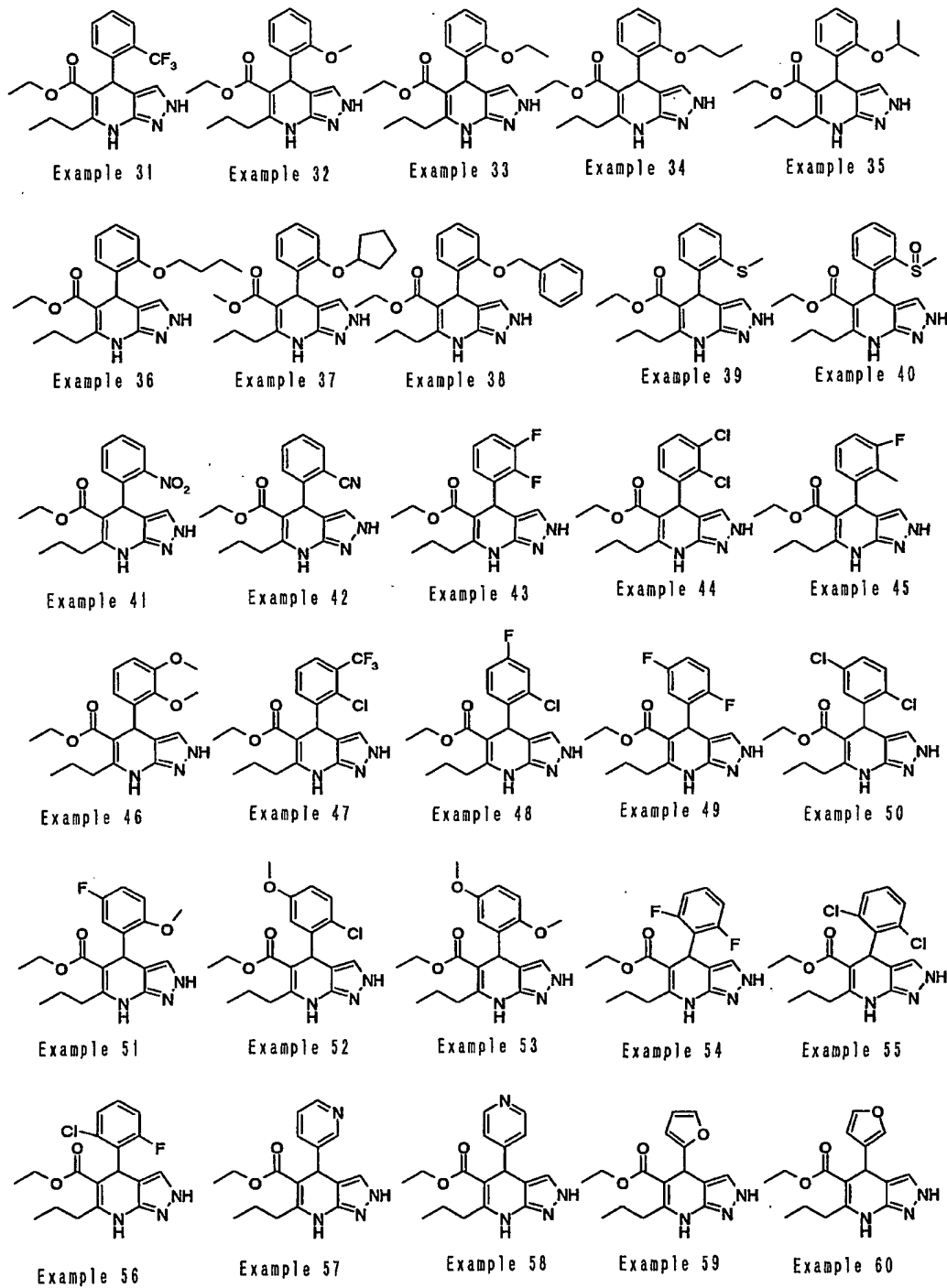
15 Found:C,65.07;H,5.05;N,21.24.

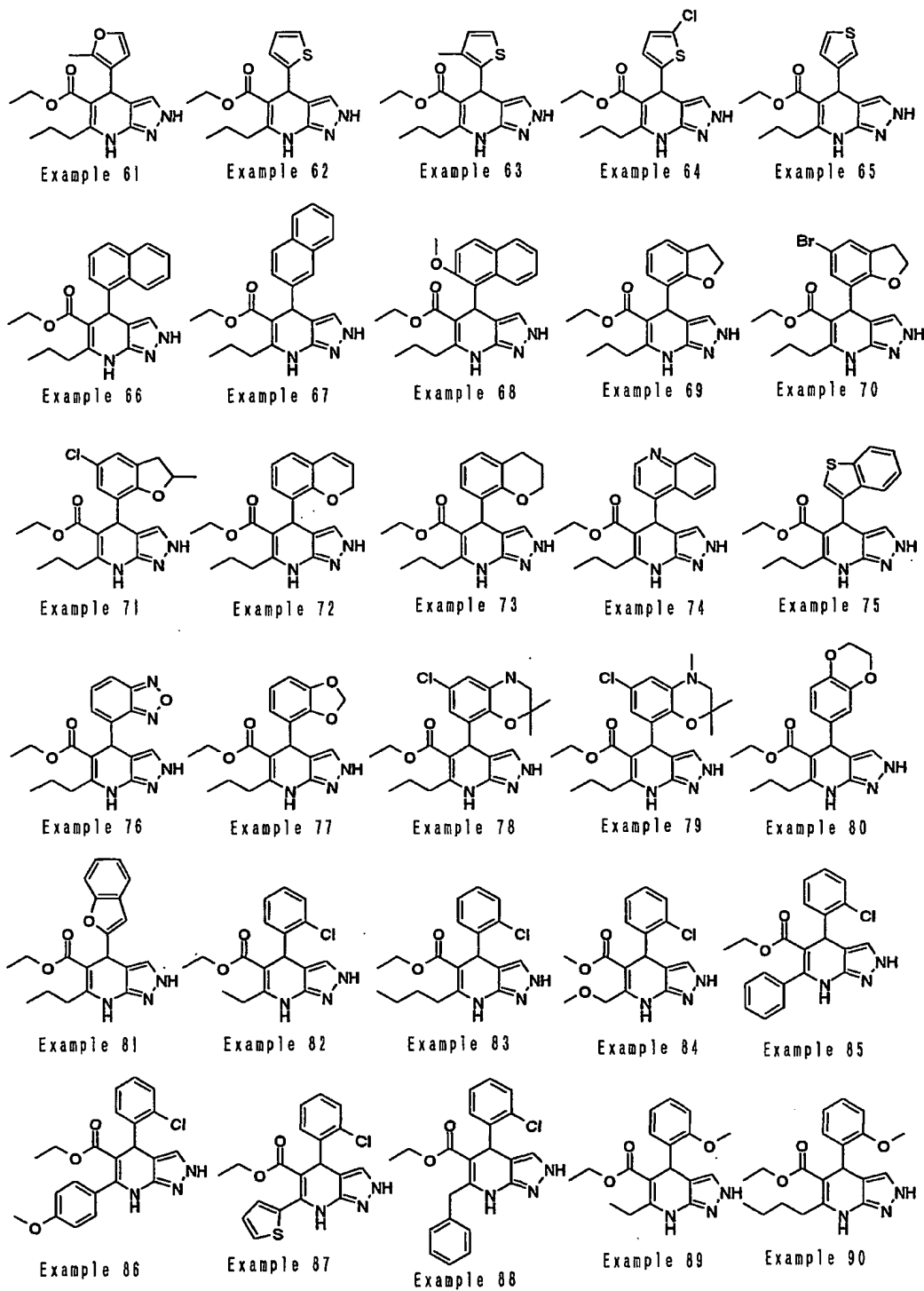
MS(EI):425(M⁺).

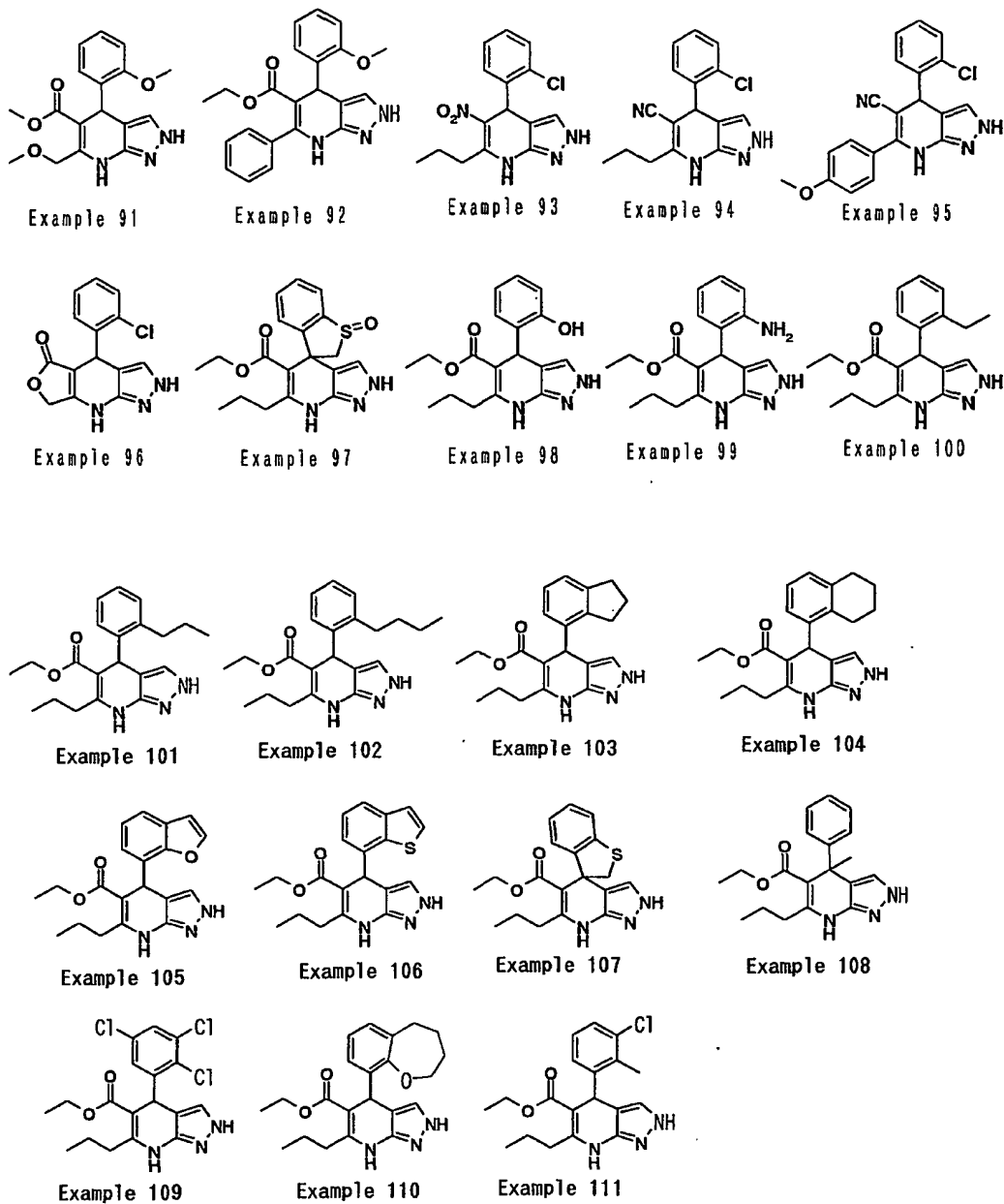
¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.91(3H,t,J=7.3Hz), 1.62(2H,m),
2.58(2H,m), 5.47(1H,s), 7.13(1H,dd,J=6.3 and 6.6Hz), 7.32-
7.39(3H,m), 7.49(1H,d,J=6.5Hz), 7.61-7.91(3H,m),
20 7.98(1H,d,J=9.1Hz), 9.54(1H,s), 10.34(1H,s).

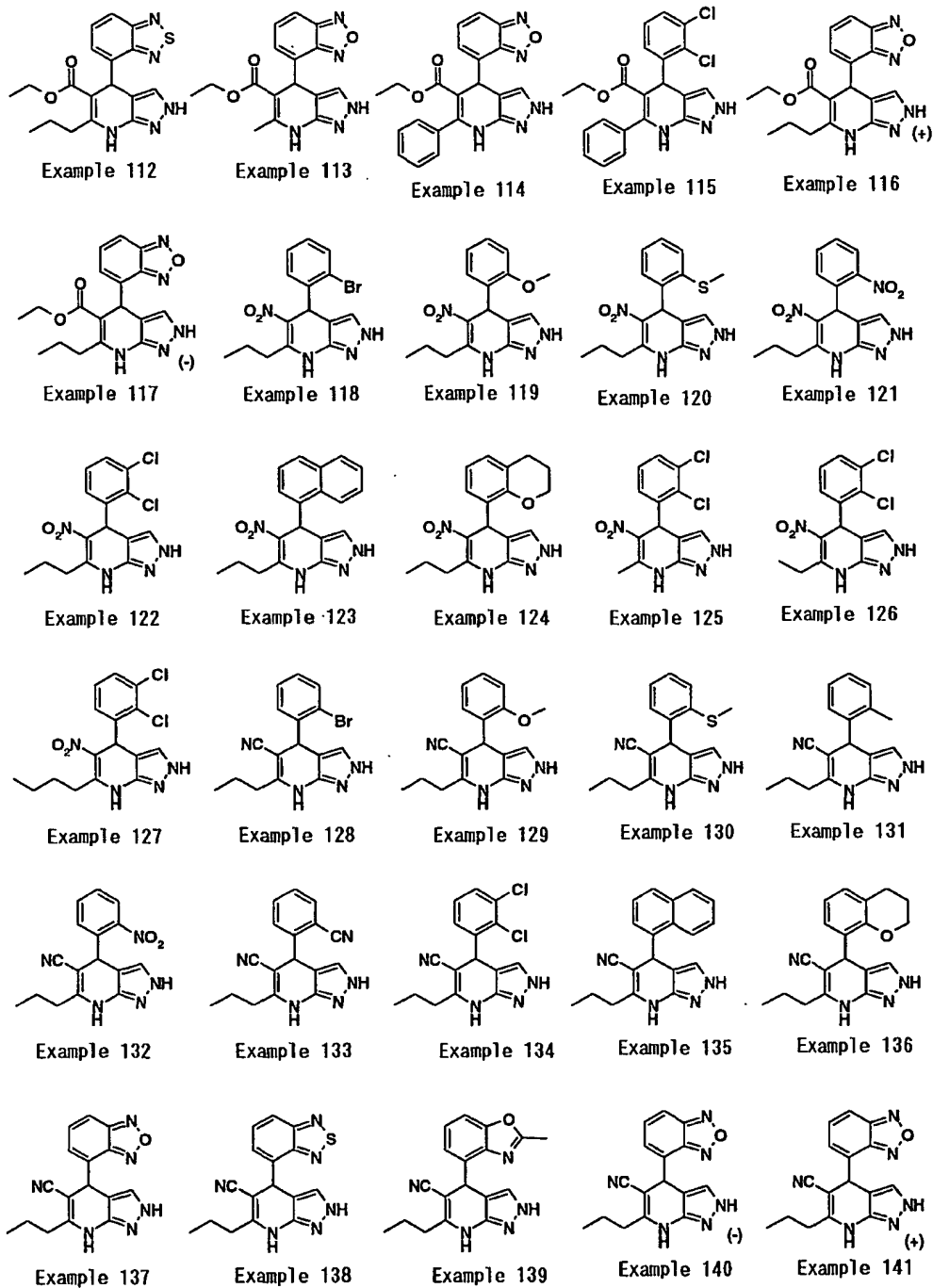
The compounds of the above-described Examples are as follows.

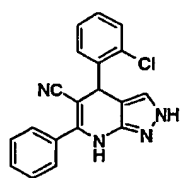




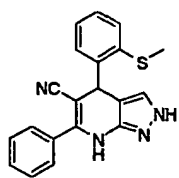




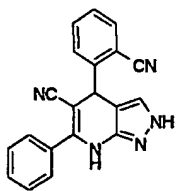




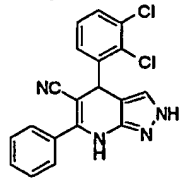
Example 142



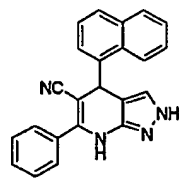
Example 143



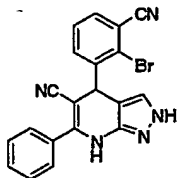
Example 144



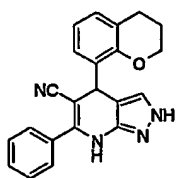
Example 145



Example 146



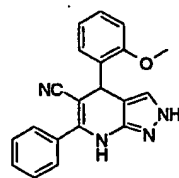
Example 147



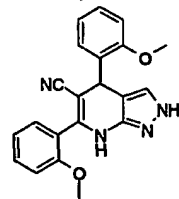
Example 148



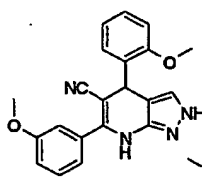
Example 149



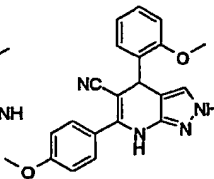
Example 150



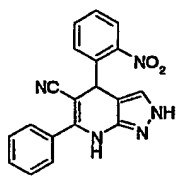
Example 151



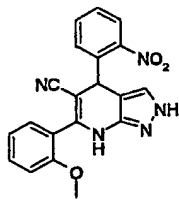
Example 152



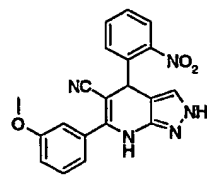
Example 153



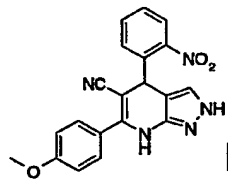
Example 154



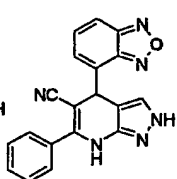
Example 155



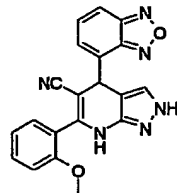
Example 156



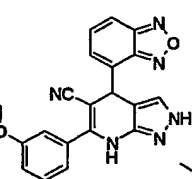
Example 157



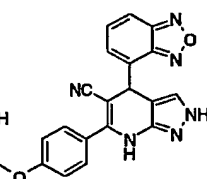
Example 158



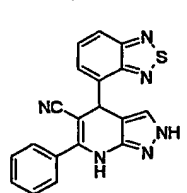
Example 159



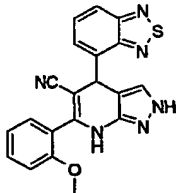
Example 160



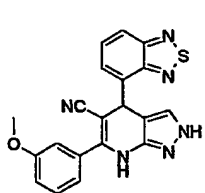
Example 161



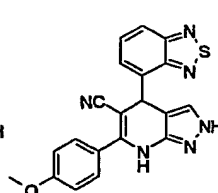
Example 162



Example 163



Example 164



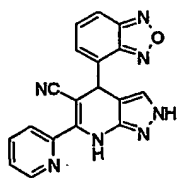
Example 165



Example 166



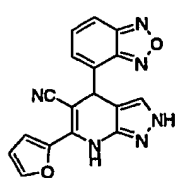
Example 167



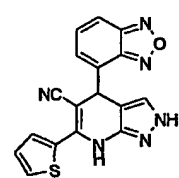
Example 168



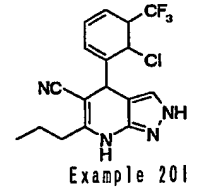
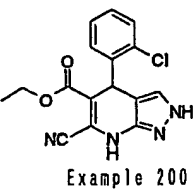
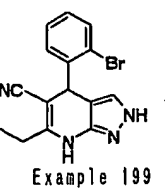
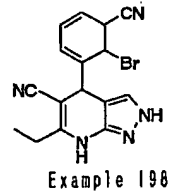
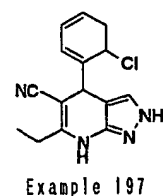
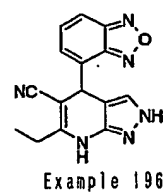
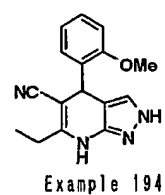
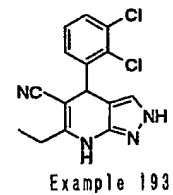
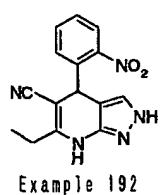
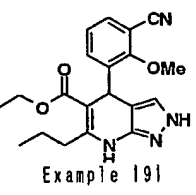
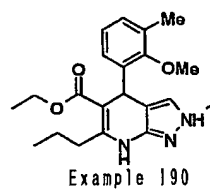
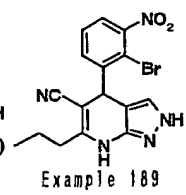
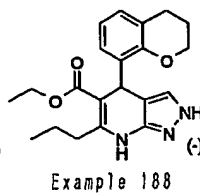
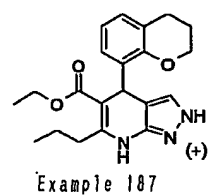
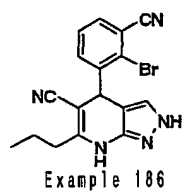
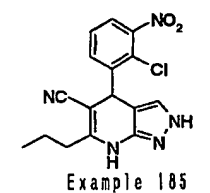
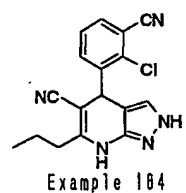
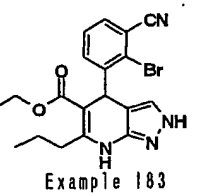
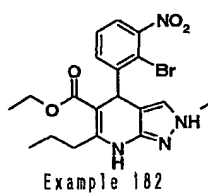
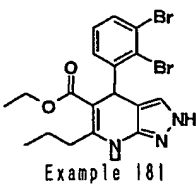
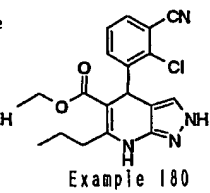
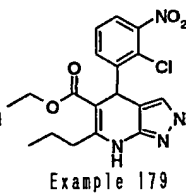
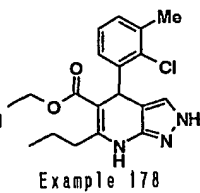
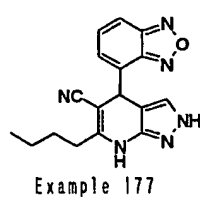
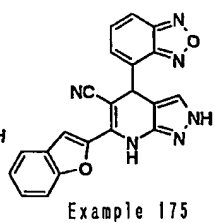
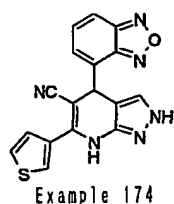
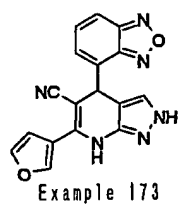
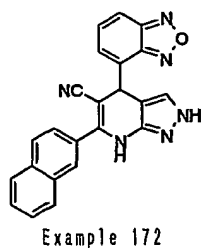
Example 169

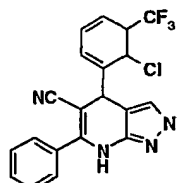


Example 170

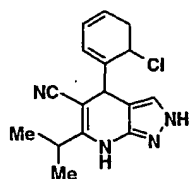


Example 171

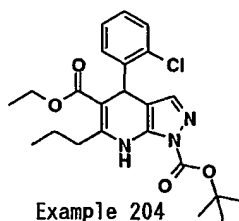




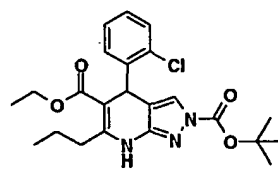
Example 202



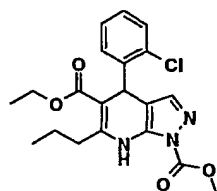
Example 203



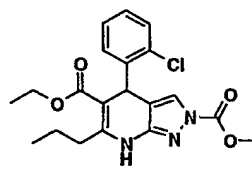
Example 204



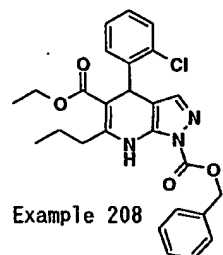
Example 205



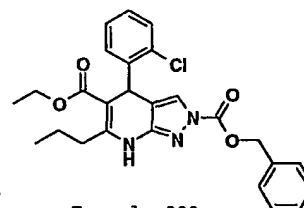
Example 206



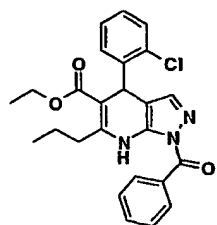
Example 207



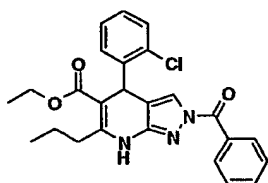
Example 208



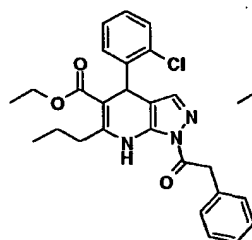
Example 209



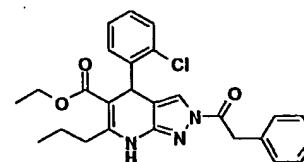
Example 210



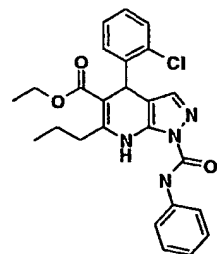
Example 211



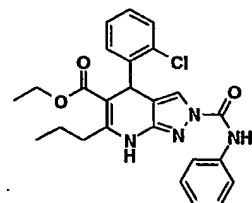
Example 212



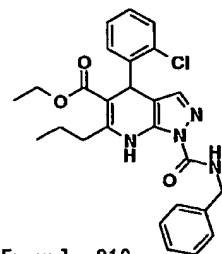
Example 213



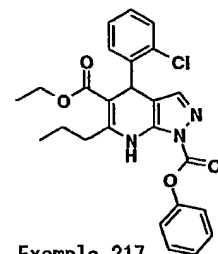
Example 214



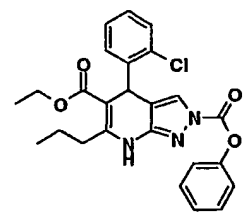
Example 215



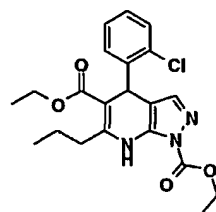
Example 216



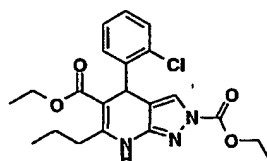
Example 217



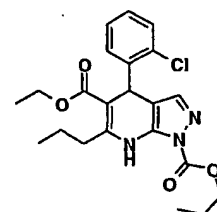
Example 218



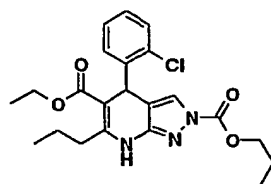
Example 219



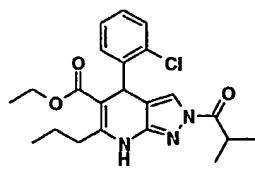
Example 220



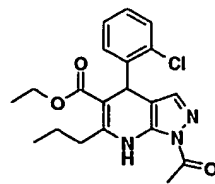
Example 221



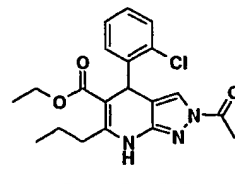
Example 222



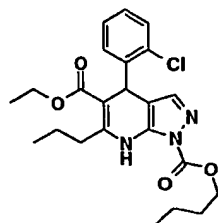
Example 223



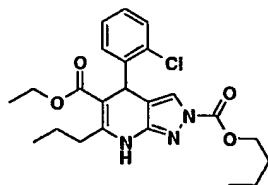
Example 224



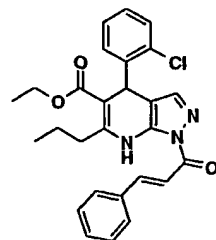
Example 225



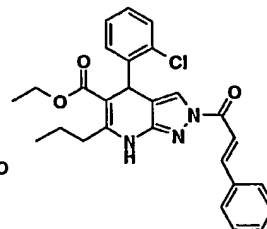
Example 226



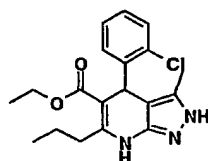
Example 227



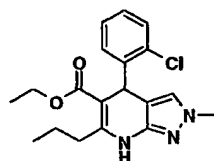
Example 228



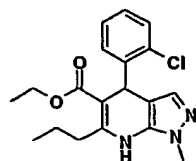
Example 229



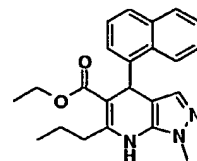
Example 230



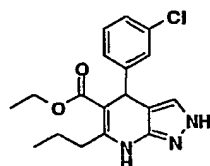
Example 231



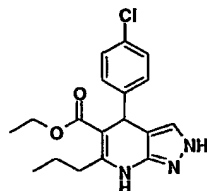
Example 232



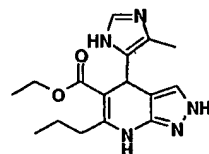
Example 233



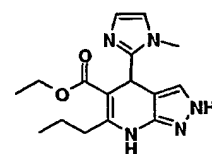
Example 234



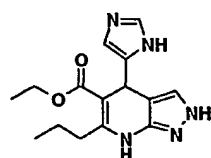
Example 235



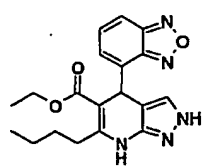
Example 236



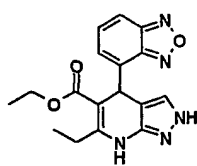
Example 237



Example 238



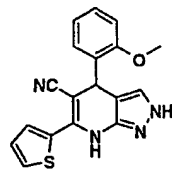
Example 239



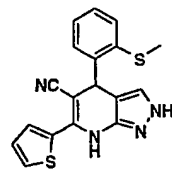
Example 240



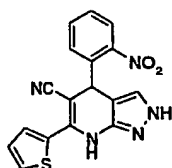
Example 241



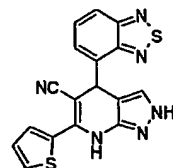
Example 242



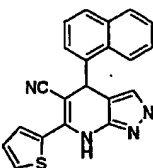
Example 243



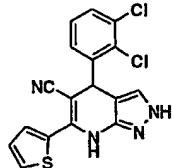
Example 244



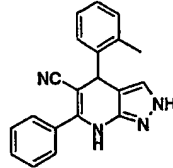
Example 245



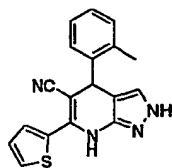
Example 246



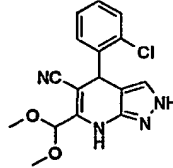
Example 247



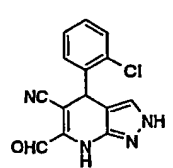
Example 248



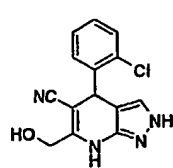
Example 249



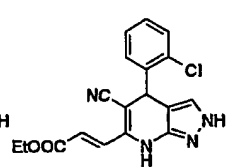
Example 250



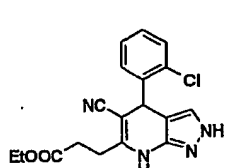
Example 251



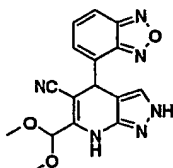
Example 252



Example 253



Example 254



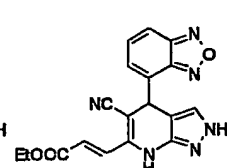
Example 255



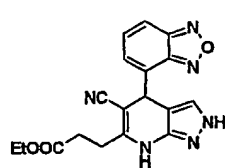
Example 256



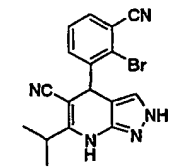
Example 257



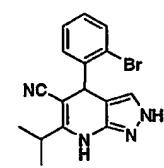
Example 258



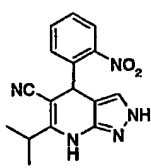
Example 259



Example 260



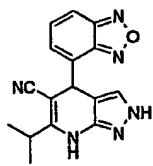
Example 261



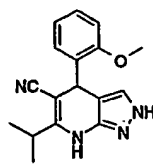
Example 262



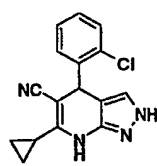
Example 263



Example 264



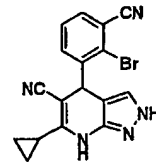
Example 265



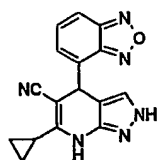
Example 266



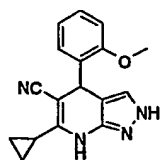
Example 267



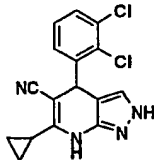
Example 268



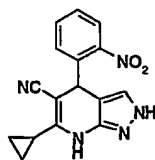
Example 269



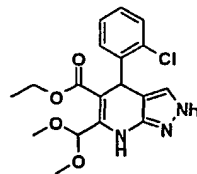
Example 270



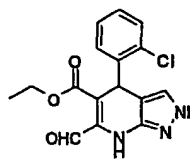
Example 271



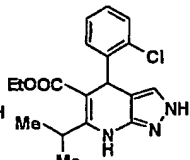
Example 272



Example 273



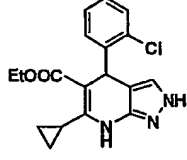
Example 274



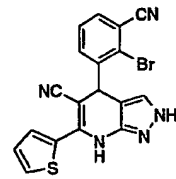
Example 275



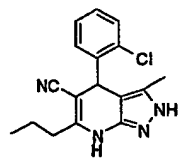
Example 276



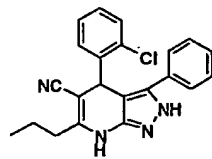
Example 277



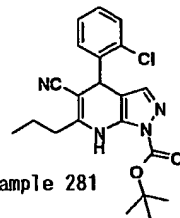
Example 278



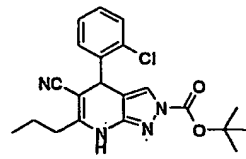
Example 279



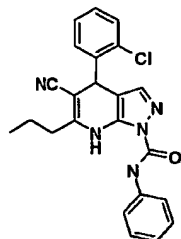
Example 280



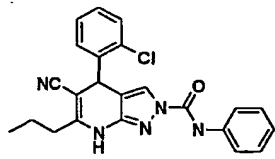
Example 281



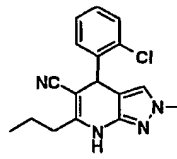
Example 282



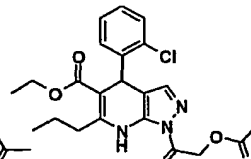
Example 283



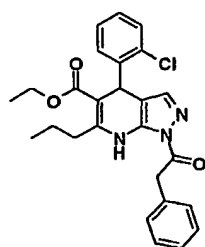
Example 284



Example 285



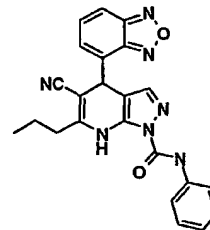
Example 286



Example 287



Example 288



Example 289

Example 2904-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(4-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (15 g) in DMSO (25 mL) was
5 added methyl p-anisate (25 g) and the mixture was stirred with
heating at 60°C for 1 hour. The reaction mixture was allowed
to cool and cold water (100 mL) was added dropwise. The
mixture was acidified with hydrochloric acid and the
precipitated crystals were collected by filtration. The
10 obtained crystals were extracted with ethyl acetate and the
solvent was evaporated under reduced pressure. The residue was
recrystallized from ethyl acetate to give 4-
methoxybenzoylacetonitrile (21 g) as colorless crystals. To a
solution of the obtained crystals in toluene was added
15 hydrazine monohydrate (13 g) and the mixture was heated under
reflux for 3 hours. The mixture was cooled and the
precipitated crystals were collected by filtration to give 5-
amino-3-(4-methoxyphenyl)pyrazole (22 g). Subsequently, the
title compound was prepared from methyl butyrate, 2-
20 chlorobenzaldehyde and 5-amino-3-(4-methoxyphenyl)pyrazole in
the same manner as in Example 94.

MP:284°C.

Anal. Calcd. for: C₂₃H₂₁ClN₄O: C, 68.23; H, 5.23; N, 13.84.

Found: C, 68.17; H, 5.29; N, 13.86.

25 MS(EI): 404(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H, t, J=7.3Hz), 1.58-
1.63(2H, m), 2.32-2.38(2H, m), 3.70(3H, s), 5.56(1H, s),
6.81(2H, d, J=7.2Hz), 7.09-7.12(2H, m), 7.17(1H, dd, J=7.3Hz and
7.2Hz), 7.24-7.30(3H, m), 9.85(1H, brs), 12.46(1H, brs).

30 Example 2914-(2,1,3-Benzoxadiazol-4-yl)-6-(2-bromothiophen-5-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 5-

bromothiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:208°C.

Anal. Calcd. for: C₁₇H₉BrN₆OS: C, 48.01; H, 2.13; N, 19.76.

5 Found: C, 47.94; H, 2.36; N, 19.78.

MS(EI): 425(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.54(1H, s), 7.32-7.34(2H, m), 7.42(1H, d, J=3.9Hz), 7.50(1H, d, J=6.6Hz), 7.61(1H, dd, J=9.0Hz), 7.95(1H, d, J=9.0Hz), 10.32(1H, brs), 12.32(1H, brs).

10 **Example 292**

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(3-methylthiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3-methylthiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:202°C.

Anal. Calcd. for: C₁₈H₁₂N₆OS: C, 59.99; H, 3.36; N, 23.32.

Found: C, 59.89; H, 3.53; N, 23.06.

MS(EI): 360(M⁺).

20 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 2.17(3H, s), 5.54(1H, s), 6.96(1H, d, J=5.1Hz), 7.32(1H, s), 7.49(1H, d, J=6.6Hz), 7.60-7.64(2H, m), 7.96(1H, d, J=9.0Hz), 10.19(1H, brs), 12.25(1H, brs).

Example 293

25 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(1-methoxymethylindol-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 1-methoxymethylindol-3-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

30 MP:200°C.

MS(EI): 423(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 3.19(3H, s), 5.55-5.63(3H, m), 7.15(1H, dd, J=7.3Hz and 7.2Hz), 7.25(1H, dd, J=7.3Hz and 7.2Hz),

7.34(1H,s), 7.54(1H,d,J=7.3Hz), 7.60-7.66(3H,m), 7.93-7.97(2H,m), 10.12(1H,brs), 12.22(1H,brs).

Example 294

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-3-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl thiophene-2-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:256°C.

10 Anal. Calcd. for: C₂₀H₁₇ClN₄S: C, 63.07; H, 4.50; N, 14.71.

Found: C, 62.98; H, 4.52; N, 14.68.

MS(EI): 380 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.86(3H,t,J=7.3Hz), 1.56-1.62(2H,m), 2.31-2.36(2H,m), 5.46(1H,s), 7.00-7.24(5H,m),
15 7.36(1H,d,J=7.3Hz), 7.50(1H,d,J=4.9Hz), 9.95(1H,brs),
12.74(1H,brs).

Example 295

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(furan-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl furan-2-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:253°C.

Anal. Calcd. for: C₂₀H₁₇ClN₄O: C, 65.84; H, 4.70; N, 15.36.

25 Found: C, 65.81; H, 4.84; N, 15.49.

MS(EI): 364 (M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H,t,J=7.3Hz), 1.58-1.63(2H,m), 2.32-2.36(2H,m), 5.48(1H,s), 6.31(1H,d,J=3.2Hz),
6.45(1H,d,J=1.5Hz), 7.14-7.23(3H,m), 7.36(1H,d,J=7.3Hz),
30 7.59(1H,s), 9.93(1H,brs), 12.76(1H,brs).

Example 296

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 2-methoxybenzoate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:>270°C.

5 Anal. Calcd. for: C₂₃H₂₁ClN₄O: C, 68.23; H, 5.23; N, 13.84.

Found: C, 68.23; H, 5.31; N, 13.87.

MS(EI): 404(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90(3H, t, J=7.3Hz), 1.60-1.65(2H, m), 2.32-2.36(2H, m), 3.70(3H, s), 5.41(1H, s),
10 6.76(1H, dd, J=7.3Hz and 7.2Hz), 6.90-6.94(2H, m), 6.98-7.04(2H, m), 7.08-7.15(2H, m), 7.22(1H, dd, J=7.3Hz and 7.2Hz), 9.83(1H, brs), 12.21(1H, brs).

Example 297

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(3-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine
15

The title compound was prepared from methyl 3-methoxybenzoate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 290.

MP:239°C.

20 Anal. Calcd. for: C₂₃H₂₁ClN₄O: C, 68.23; H, 5.23; N, 13.84.

Found: C, 68.16; H, 5.31; N, 13.80.

MS(EI): 404(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.88(3H, t, J=7.3Hz), 1.58-1.63(2H, m), 2.31-2.36(2H, m), 3.68(3H, s), 6.78(1H, d, J=7.3Hz),
25 6.87-6.89(2H, m), 7.11-7.20(4H, m), 7.29(1H, d, J=7.3Hz), 9.92(1H, brs), 12.64(1H, brs).

Example 298

4-(2,1,3-Benzoxadiazol-4-yl)-6-(2-chlorothiophen-5-yl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine
30

The title compound was prepared from methyl 5-chlorothiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:210°C.

Anal. Calcd. for: $C_{17}H_9ClN_6OS$: C, 53.62; H, 2.38; N, 22.07.

Found: C, 53.51; H, 2.67; N, 22.13.

MS(EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.54(1H, s), 7.23(1H, d, J=3.9Hz),
5 7.33(1H, s), 7.46(1H, d, J=3.9Hz), 7.50(1H, d, J=6.6Hz),
7.60(1H, dd, J=9.0Hz and 6.6Hz), 7.95(1H, d, J=9.0Hz),
10.31(1H, brs), 12.30(1H, brs).

Example 299

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(2-
10 methylthiophen-5-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 5-methylthiophene-2-carboxylate, 2,1,3-benzoxadiazol-4-aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP: 192°C.

15 MS(EI): 360 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.50(3H, s), 5.52(1H, s),
6.87(1H, d, J=3.6Hz), 7.32(1H, s), 7.40(1H, d, J=3.7Hz),
7.48(1H, d, J=6.6Hz), 7.61(1H, dd, J=9.0Hz and 6.6Hz),
7.95(1H, d, J=9.0Hz), 10.12(1H, brs), 12.26(1H, brs).

20 Example 300

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(naphthalen-1-yl)-6-
propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl naphthalene-1-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the
25 same manner as in Example 290.

MP: 254°C.

Anal. Calcd. for: $C_{26}H_{21}ClN_4$: C, 73.49; H, 4.98; N, 13.19.

Found: C, 73.81; H, 5.05; N, 13.08.

MS(EI): 424 (M^+).

30 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, J=7.3Hz), 1.64-
1.70(2H, m), 2.46-2.49(2H, m), 5.25(1H, s), 6.88-7.02(5H, m),
7.31(1H, dd, J=7.3Hz and 7.2Hz), 7.42-7.47(3H, m), 7.83-
7.88(2H, m), 9.95(1H, brs), 12.46(1H, brs).

Example 3014-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(naphthalen-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl naphthalene-
5 2-carboxylate, methyl butyrate and 2-chlorobenzaldehyde in the
same manner as in Example 290.

MP:>270°C.

Anal. Calcd. for: C₂₆H₂₁ClN₄: C, 73.49; H, 4.98; N, 13.19.

Found: C, 73.23; H, 5.01; N, 13.26.

10 MS(EI): 424(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.91(3H, t, J=7.3Hz), 1.61-
1.66(2H, m), 2.31-2.41(2H, m), 5.76(1H, s), 7.05(1H, dd, J=7.3Hz
and 7.2Hz), 7.12-7.16(2H, m), 7.28(1H, d, J=7.3Hz), 7.45-
7.52(2H, m), 7.57(1H, d, J=7.3Hz), 7.77-7.84(4H, m), 9.94(1H, brs),
15 12.79(1H, brs).

Example 3024-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3,6-dipropyl-2H-pyrazolo[3,4-b]pyridine

To a solution of acetonitrile (4.8 g) in THF (150 mL)
20 was added n-BuLi (67 mmol) at -78°C. Methyl butyrate (10 g)
was added and the mixture was stirred for 1 hour. The reaction
mixture was acidified with hydrochloric acid and extracted
with ethyl acetate. The solvent was evaporated under reduced
pressure and the residue was purified by silica gel column
25 chromatography (eluent: hexane-ethyl acetate (10:1)) to give
1-cyanopentan-2-one (5.5 g) as a colorless oil. To a solution
of the obtained colorless oil in toluene was added hydrazine
monohydrate (5.0 g) and the mixture was heated under reflux
for 3 hours. The mixture was cooled and the solvent was
30 evaporated under reduced pressure. The reaction mixture was
purified by silica gel column chromatography (eluent:
chloroform-methanol (10:1)) to give 5-amino-3-propylpyrazole
(5.0 g). A solution of 2-chloroaldehyde (1.7 g), 5-amino-3-

propylpyrazole (1.5 g) and 1-cyanopentan-2-one (1.6 g) in acetonitrile (20 mL) was heated under reflux overnight. The mixture was cooled to room temperature and the precipitated crystals were collected by filtration to give the title
5 compound (2.1 g) as colorless crystals.

MP:237°C.

Anal. Calcd. for: $C_{19}H_{21}ClN_4$: C, 66.95; H, 6.21; N, 16.44.

Found: C, 66.98; H, 6.26; N, 16.41.

MS(EI): 340 (M^+).

10 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.57(3H, t, J=7.3Hz),
0.91(3H, t, J=7.3Hz), 1.02-1.07(2H, m), 1.59-1.65(2H, m), 2.01-
2.12(2H, m), 2.30-2.38(2H, m), 5.28(1H, s), 7.20-7.23(2H, m),
7.30(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz),
9.70(1H, brs), 11.85(1H, brs).

15 **Example 303**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-hydroxy-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 2-chlorobenzaldehyde and 3-amino-5-hydroxypyrazole in the same
20 manner as in Example 94.

MS(EI): 314 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.89(3H, t, J=7.3Hz), 1.56-
1.60(2H, m), 2.26-2.38(2H, m), 5.11(1H, s), 7.14-7.21(3H, m),
7.27(1H, dd, J=7.3Hz and 7.2Hz), 7.34(1H, d, J=7.3Hz),
25 9.64(1H, brs), 10.45(1H, brs).

Example 304

3-Butyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pentanoate,
30 methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:212°C.

Anal. Calcd. for: $C_{20}H_{23}ClN_4$: C, 67.69; H, 6.53; N, 15.79.

Found: C, 67.58; H, 6.46; N, 15.75.

MS(EI): 354(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.64(3H, t, J=7.3Hz), 0.89-
0.98(6H, m), 1.10-1.14(1H, m), 1.59-1.64(2H, m), 2.05-2.16(2H, m),
5 2.31-2.35(2H, m), 5.28(1H, s), 7.20-7.24(2H, m),
7.29(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz),
9.70(1H, brs), 11.85(1H, brs).

Example 305

4-(2,1,3-Benzoxadiazol-4-yl)-6-(benzothiophen-2-yl)-5-cyano-
10 4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
benzothiophene-2-carboxylate, 2,1,3-benzoxadiazole-4-aldehyde
and 3-aminopyrazole in the same manner as in Example 95.

MP: 220°C.

15 Anal. Calcd. for: C₂₁H₁₂N₆OS: C, 63.62; H, 3.05; N, 21.20.

Found: C, 63.58; H, 3.29; N, 21.09.

MS(EI): 396(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 5.60(1H, s), 7.36(1H, s), 7.44-
7.46(2H, m), 7.54(1H, d, J=6.3Hz), 7.64(1H, dd, J=9.0Hz and 6.6Hz),
20 7.88(1H, s), 7.94-7.98(2H, m), 8.05(1H, d, J=9.0Hz), 10.40(1H, brs),
12.31(1H, brs).

Example 306

4-(2-Chlorophenyl)-5-cyano-6-cyclohexyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl
cyclohexanecarboxylate, 2-chlorobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP: 163°C.

Anal. Calcd. for: C₁₉H₁₉ClN₄ 1/2 H₂O: C, 65.61; H, 5.80; N, 16.11.

30 Found: C, 65.40; H, 5.77; N, 15.86.

MS(EI): 338(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.16-1.30(3H, m), 1.66-1.85(7H, m),
2.66-2.72(1H, m), 5.33(1H, s), 7.21-7.25(3H, m),

7.32(1H,dd,J=7.3Hz and 7.2Hz), 7.41(1H,d,J=7.3Hz),
9.60(1H,brs), 12.15(1H,brs).

Example 307

6-t-Butyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo

5 [3,4-b]pyridine

The title compound was prepared from methyl pivalate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:198°C.

10 Anal. Calcd. for: C₁₇H₁₇ClN₄: C, 65.28; H, 5.48; N, 17.91.

Found: C, 64.98; H, 5.47; N, 17.78.

MS(EI): 312(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.41(9H,s), 5.33(1H,s), 7.21-7.33(4H,m), 7.41(1H,d,J=7.3Hz), 8.88(1H,brs), 12.20(1H,brs).

15 **Example 308**

4-(2-Chlorophenyl)-5-cyano-3-cyclopropyl-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopropanecarboxylate, methyl butyrate and 2-

20 chlorobenzaldehyde in the same manner as in Example 302.

MP:270°C.

Anal. Calcd. for: C₁₉H₁₉ClN₄: C, 67.35; H, 5.65; N, 16.54.

Found: C, 67.34; H, 5.66; N, 16.62.

MS(EI): 338(M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.22-0.25(1H,m), 0.41-0.44(1H,m), 0.50-0.54(1H,m), 0.62-0.66(1H,m), 0.90(3H,t,J=7.3Hz), 1.25-1.29(1H,m), 1.58-1.63(2H,m), 2.31-2.36(2H,m), 5.33(1H,s), 7.18-7.23(2H,m), 7.30(1H,dd,J=7.3Hz and 7.2Hz), 7.38(1H,d,J=7.3Hz), 9.69(1H,brs), 11.73(1H,brs).

30 **Example 309**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-ethyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl propionate,

methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:269°C.

Anal. Calcd. for: C₁₈H₁₉ClN₄: C, 66.15; H, 5.86; N, 17.14.

5 Found: C, 66.27; H, 5.86; N, 17.25.

MS(EI): 326(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.72(3H, t, J=7.3Hz),
0.91(3H, t, J=7.3Hz), 1.59-1.64(2H, m), 2.09-2.11(2H, m), 2.31-
2.40(2H, m), 5.29(1H, s), 7.20-7.24(2H, m), 7.30(1H, dd, J=7.3Hz
10 and 7.2Hz), 7.38(1H, d, J=7.3Hz), 9.70(1H, brs), 11.86(1H, brs).

Example 310

3-t-Butyl-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pivalate,
15 methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:>270°C.

Anal. Calcd. for: C₂₀H₂₃ClN₄: C, 67.69; H, 6.53; N, 15.79.

Found: C, 67.55; H, 6.56; N, 15.66.

20 MS(EI): 354(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.84(3H, t, J=7.3Hz), 0.95(9H, s),
1.53-1.59(2H, m), 2.26-2.30(2H, m), 5.39(1H, s),
6.97(1H, d, J=7.3Hz), 7.20(1H, dd, J=7.3Hz and 7.2Hz),
7.27(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz),
25 9.73(1H, brs), 11.87(1H, brs).

Example 311

4-(2-Chlorophenyl)-5-cyano-3-cyclohexyl-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
30 cyclohexanecarboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:>270°C.

Anal. Calcd. for: C₂₂H₂₅ClN₄: C, 69.37; H, 6.62; N, 14.71.

Found: C, 69.17; H, 6.62; N, 14.91.

MS(EI): 380(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89-1.17(9H, m), 1.47-1.64(6H, m),
2.06-2.08(1H, m), 2.31-2.38(2H, m), 5.30(1H, s), 7.19-7.23(2H, m),
5 7.29(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz),
9.71(1H, brs), 11.83(1H, brs).

Example 312

4-(2-Chlorophenyl)-5-cyano-6-cycloheptyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl
cycloheptanecarboxylate, 2-chlorobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP: 146°C.

MS(EI): 352(M⁺).

15 ¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.42-1.98(12H, m), 2.78-
2.81(1H, m), 5.33(1H, s), 7.21-7.24(3H, m), 7.32(1H, dd, J=7.3Hz
and 7.2Hz), 7.41(1H, d, J=7.3Hz), 9.61(1H, brs), 12.18(1H, brs).

Example 313

4-(2-Chlorophenyl)-5-cyano-6-cyclobutyl-4,7-dihydro-2H-
20 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
cyclobutanecarboxylate, 2-chlorobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP: 188°C.

25 Anal. Calcd. for: C₁₇H₁₅ClN₄: C, 65.70; H, 4.86; N, 18.03.

Found: C, 65.51; H, 5.21; N, 18.27.

MS(EI): 310(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.72-1.77(1H, m), 1.93-1.97(1H, m),
2.09-2.12(2H, m), 2.38-2.43(2H, m), 2.58-2.61(1H, m), 5.33(1H, s),
30 7.20-7.32(4H, m), 7.41(1H, d, J=7.3Hz), 9.72(1H, brs),
12.18(1H, brs).

Example 314

4-(2-Chlorophenyl)-5-cyano-3-cyclopentyl-4,7-dihydro-6-propyl-

2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopentanecarboxylate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

5 MP:>270°C.

Anal. Calcd. for: C₂₁H₂₃ClN₄: C, 68.75; H, 6.32; N, 15.27.

Found: C, 68.56; H, 6.36; N, 15.22.

MS(EI): 366(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.89(3H, t, J=7.3Hz), 1.31-
10 1.74(10H, m), 2.30-2.37(2H, m), 2.52-2.54(1H, m),
5.30(1H, s), 7.17-7.22(2H, m), 7.28(1H, dd, J=7.3Hz and 7.2Hz),
7.37(1H, d, J=7.3Hz), 9.71(1H, brs), 11.86(1H, brs).

Example 3154-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-3-isopropyl-15 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 2-methylpropionate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:>270°C.

20 Anal. Calcd. for: C₁₉H₂₁ClN₄: C, 66.95; H, 6.21; N, 16.44.

Found: C, 66.90; H, 6.27; N, 16.44.

MS(EI): 340(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.67(3H, d, J=7.2Hz),
0.90(3H, t, J=7.3Hz), 0.95(3H, d, J=7.3Hz), 1.57-1.63(2H, m), 2.30-
25 2.35(2H, m), 5.30(1H, s), 7.19-7.23(2H, m), 7.29(1H, dd, J=7.3Hz
and 7.2Hz), 7.38(1H, d, J=7.3Hz), 9.71(1H, brs), 11.88(1H, brs).

Example 3164-(2-Chlorophenyl)-5-cyano-6-cyclopentyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl cyclopentanecarboxylate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:225°C.

Anal. Calcd. for: $C_{18}H_{17}ClN_4 \cdot 1/5 H_2O$: C, 65.83; H, 5.34; N, 17.06.

Found: C, 66.02; H, 5.51; N, 16.62.

MS(EI): 324 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.56-1.60 (2H, m), 1.78-1.87 (6H, m),
5 3.06-3.10 (1H, m), 5.34 (1H, s), 7.22-7.26 (3H, m),
7.32 (1H, dd, $J=7.3$ Hz and 7.2Hz), 7.42 (1H, d, $J=7.3$ Hz),
9.61 (1H, brs), 12.16 (1H, brs).

Example 317

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclopentyl-4,7-dihydro-
10 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopentanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 247°C.

15 MS(EI): 394 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.52-1.58 (2H, m), 1.75-1.82 (6H, m),
3.01-3.06 (1H, m), 5.46 (1H, s), 7.33 (1H, s), 7.54-7.58 (2H, m),
7.84 (1H, d, $J=7.3$ Hz), 9.73 (1H, brs), 12.25 (1H, brs).

Example 318

20 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclopentyl-4,7-
dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclopentanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

25 MP: 193°C.

Anal. Calcd. for: $C_{18}H_{16}N_6O$: C, 65.05; H, 4.85; N, 25.29.

Found: C, 64.72; H, 4.98; N, 24.86.

MS(EI): 332 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.55-1.58 (2H, m), 1.80-1.86 (6H, m),
30 3.06-3.09 (1H, m), 5.39 (1H, s), 7.26 (1H, s), 7.38 (1H, d, $J=6.6$ Hz),
7.60 (1H, dd, $J=9.0$ Hz and 6.6Hz), 7.91 (1H, d, $J=9.0$ Hz),
9.72 (1H, brs), 12.15 (1H, brs).

Example 319

4-(2-Bromo-3-cyanophenyl)-6-t-butyl-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pivalate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:251°C.

Anal. Calcd. for: $C_{18}H_{16}BrN_5 \cdot 1/2 H_2O$: C, 55.25; H, 4.38; N, 17.90.

Found: C, 55.55; H, 4.30; N, 18.14.

10 MS(EI): 382(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.41(9H, s), 5.46(1H, s), 7.33(1H, s), 7.54-7.60(2H, m), 7.82(1H, d, J=7.3Hz), 9.00(1H, brs), 12.29(1H, brs).

Example 320

15 4-(2,1,3-Benzoxadiazol-4-yl)-6-t-butyl-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl pivalate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

20 MP:204°C.

Anal. Calcd. for: $C_{17}H_{16}N_6O \cdot 1/2 H_2O$: C, 63.03; H, 5.10; N, 25.94.

Found: C, 63.08; H, 5.08; N, 26.00.

MS(EI): 320(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.40(9H, s), 5.37(1H, s), 25 7.26(1H, s), 7.38(1H, d, J=6.6Hz), 7.59(1H, dd, J=9.0Hz and 6.6Hz), 7.91(1H, d, J=9.0Hz), 9.02(1H, brs), 12.20(1H, brs).

Example 321

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclobutyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

30 The title compound was prepared from methyl cyclobutanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:278°C.

Anal. Calcd. for: $C_{18}H_{14}BrN_5$: C, 56.86; H, 3.71; N, 18.42.

Found: C, 56.57; H, 3.79; N, 18.48.

MS(EI): 380 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.71(1H, m), 1.88-1.95(1H, m),
5 2.06-2.13(2H, m), 2.38-2.47(2H, m), 3.56-3.60(1H, m), 5.45(1H, s),
7.33(1H, s), 7.57-7.59(2H, m), 7.82(1H, d, $J=7.3$ Hz), 9.84(1H, brs),
12.27(1H, brs).

Example 322

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclobutyl-4,7-dihydro-
10 2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl cyclobutanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 194°C.

15 Anal. Calcd. for: $C_{17}H_{14}N_6O$: C, 64.14; H, 4.43; N, 26.40.

Found: C, 64.08; H, 4.51; N, 26.26.

MS(EI): 318 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.72-1.76(1H, m), 1.90-1.97(1H, m),
2.10-2.14(2H, m), 2.39-2.46(2H, m), 3.56-3.60(1H, m), 5.38(1H, s),
20 7.26(1H, s), 7.37(1H, d, $J=6.6$ Hz), 7.58(1H, dd, $J=9.0$ Hz and 6.6Hz),
7.91(1H, d, $J=9.0$ Hz), 9.82(1H, brs), 12.17(1H, brs).

Example 323

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cyclohexyl-4,7-dihydro-
2H-pyrazolo[3,4-b]pyridine

25 The title compound was prepared from methyl cyclohexanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP: 210°C.

Anal. Calcd. for: $C_{19}H_{18}N_6O$: C, 65.88; H, 5.24; N, 24.26.

30 Found: C, 65.88; H, 5.25; N, 24.19.

MS(EI): 346 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.21-1.26(3H, m), 1.62-1.80(7H, m),
2.66-2.70(1H, m), 5.38(1H, s), 7.25(1H, s), 7.38(1H, d, $J=6.6$ Hz),

7.59(1H,dd,J=9.0Hz and 6.6Hz), 7.91(1H,d,J=9.0Hz),
9.72(1H,brs), 12.15(1H,brs).

Example 324

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-cycloheptyl-4,7-
5 dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
cycloheptanecarboxylate, 2,1,3-benzoxadiazole-4-aldehyde and
3-aminopyrazole in the same manner as in Example 94.

MP:228°C.

10 Anal. Calcd. for: C₂₀H₂₀N₆O: C, 66.65; H, 5.59; N, 23.32.

Found: C, 66.45; H, 5.70; N, 22.97.

MS(EI): 360(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.38-1.98(12H,m), 2.76-
2.79(1H,m), 5.37(1H,s), 7.24(1H,s), 7.38(1H,d,J=6.6Hz),
15 7.58(1H,dd,J=9.0Hz and 6.6Hz), 7.91(1H,d,J=9.0Hz), 9.72(1H,brs),
12.13(1H,brs).

Example 325

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cyclohexyl-4,7-dihydro-2H-
pyrazolo[3,4-b]pyridine

20 The title compound was prepared from methyl
cyclohexanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

MP:193°C.

Anal. Calcd. for: C₂₀H₁₈BrN₅ 1/2 H₂O: C, 57.56; H, 4.59; N, 16.78.

25 Found: C, 57.25; H, 4.37; N, 16.56.

MS(EI): 408(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21-1.26(3H,m), 1.66-1.80(7H,m),
2.66-2.69(1H,m), 5.45(1H,s), 7.33(1H,s), 7.55-7.60(2H,m),
7.82(1H,d,J=7.3Hz), 9.73(1H,brs), 12.24(1H,brs).

30 Example 326

4-(2-Bromo-3-cyanophenyl)-5-cyano-6-cycloheptyl-4,7-dihydro-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl

cycloheptanecarboxylate, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:252°C.

Anal. Calcd. for: $C_{21}H_{20}BrN_5 \cdot \frac{1}{2} H_2O$: C, 58.48; H, 4.91; N, 16.24.

5 Found: C, 58.53; H, 4.73; N, 16.19.

MS(EI): 422 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.44-1.58 (12H, m), 2.76-2.79 (1H, m), 5.44 (1H, s), 7.31 (1H, s), 7.54-7.60 (2H, m), 7.83 (1H, d, J=7.3Hz), 9.73 (1H, brs), 12.23 (1H, brs).

10 **Example 327**

5-Cyano-4,7-dihydro-6-propyl-4-(pyridin-3-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, pyridine-3-aldehyde and 3-aminopyrazole in the same manner as

15 in Example 94.

MP:201°C.

Anal. Calcd. for: $C_{15}H_{15}N_5$: C, 67.90; H, 5.70; N, 26.40.

Found: C, 67.42; H, 5.74; N, 26.72.

MS(EI): 265 (M^+).

20 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.92 (3H, t, J=7.3Hz), 1.62-1.67 (2H, m), 2.36-2.39 (2H, m), 4.98 (1H, s), 7.27 (1H, s), 7.35 (1H, dd, J=7.3Hz and 2.9Hz), 7.54 (1H, d, J=7.3Hz), 8.41-8.44 (2H, m), 9.81 (1H, brs), 12.18 (1H, brs).

Example 328

25 3-t-Butoxycarbonyloxy-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-1H-pyrazolo[3,4-b]pyridine

To a solution of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-3-hydroxy-6-propyl-2H-pyrazolo[3,4-b]pyridine (12.5 g) in THF (400 mL) was added triethylamine (4.5 g),

30 dimethylaminopyridine (0.5 g) and di-t-butylcarbonate (9.6 g) and the mixture was stirred for 3 hours. The mixture was extracted with ethyl acetate and the solvent was evaporated under reduced pressure. The residue was recrystallized from

ethyl acetate to give the title compound (12 g) as colorless crystals.

MP:182°C.

Anal. Calcd. for: $C_{21}H_{23}ClN_4O_3$: C, 60.79; H, 5.59; N, 13.50.

5 Found: C, 60.60; H, 5.50; N, 13.44.

MS(EI): 414(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, J=7.3Hz), 1.54(9H, s),
2.49-2.51(2H, m), 5.18(1H, s), 7.23-7.27(2H, m),
7.32(1H, dd, J=7.3Hz and 7.2Hz), 7.38(1H, d, J=7.3Hz),
10 9.15(1H, brs), 10.99(1H, brs).

Example 329

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(2,2-dimethoxyethyl)-
4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3,3-
15 dimethoxypropionate, 2,1,3-benzoxadiazole-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:115°C.

Anal. Calcd. for: $C_{17}H_{16}N_6O_3 \cdot 1.0 H_2O$: C, 55.13; H, 4.90; N, 22.69.

Found: C, 55.30; H, 4.51; N, 22.99.

20 MS(EI): 352(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 2.71(2.75(2H, m), 3.28(3H, s),
3.31(3H, s), 4.74(1H, t, J=5.9Hz), 5.43(1H, s), 7.28(1H, s),
7.40(1H, d, J=6.6Hz), 7.61(1H, dd, J=9.0Hz and 6.6Hz),
7.92(1H, d, J=9.0Hz), 9.99(1H, brs), 12.18(1H, brs).

25 Example 330

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-(2,2-dimethoxyethyl)-
6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 3,3-
dimethoxypropionate, methyl butyrate and 2-chlorobenzaldehyde
30 in the same manner as in Example 302.

MP:180°C.

Anal. Calcd. for: $C_{20}H_{23}ClN_4O_2$: C, 62.09; H, 5.99; N, 14.48.

Found: C, 62.35; H, 6.02; N, 14.50.

MS(EI):386(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.91(3H,t,J=7.3Hz), 1.59-
1.64(2H,m), 2.28-2.35(4H,m), 3.00(3H,s), 3.02(3H,s),
3.81(1H,t,J=7.3Hz), 5.31(1H,s), 7.24-7.31(3H,m),
5 7.40(1H,d,J=7.3Hz), 9.75(1H,brs), 11.92(1H,brs).

Example 331

4-(2,1-Benzoisoxazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate,
10 2,1-benzoisoxazole-4.aldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:239°C.

MS(EI):305(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.91(3H,t,J=7.3Hz), 1.64-
15 1.67(2H,m), 2.40-2.43(2H,m), 5.23(1H,s), 6.91(1H,d,J=6.6Hz),
7.28(1H,s), 7.36(1H,dd,J=9.3Hz and 6.6Hz), 7.52(1H,d,J=9.3Hz),
9.37(1H,s), 9.96(1H,brs), 12.21(1H,brs).

Example 332

4-(2,1-Benzoisoxazol-4-yl)-5-cyano-4,7-dihydro-6-isopropyl-2H-
20 pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
2,1-benzoisoxazole-4.aldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:245°C.

25 MS(EI):305(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 1.23-1.26(6H,m),
3.03(1H,t,J=5.9Hz), 5.21(1H,s), 6.92(1H,d,J=6.6Hz), 7.30(1H,s),
7.37(1H,dd,J=9.3Hz and 6.6Hz), 7.53(1H,d,J=9.3Hz), 9.34(1H,s),
9.78(1H,brs), 12.23(1H,brs).

30 **Example 333**

4-(2,1-Benzoisoxazol-4-yl)-5-cyano-6-cyclopropyl-4,7-dihydro-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl

cyclopropanecarboxylate, 2,1-benzisoxazole-4.aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:248°C.

MS(EI):303(M⁺).

5 ¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.89-0.91(2H,m), 1.05-1.08(2H,m), 1.94-1.98(2H,m), 5.20(1H,s), 6.91(1H,d,J=6.6Hz),7.28(1H,s), 7.36(1H,dd,J=9.3Hz and 6.6Hz), 7.52(1H,d,J=9.3Hz), 9.26(1H,s), 9.36(1H,brs),12.22(1H,brs).

Example 334

10 4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-6-(1-t-butoxycarbonylindol-3-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl 1-t-butoxycarbonylindole-3-carboxylate, 2,1,3-benzoxadiazole-4-
15 aldehyde and 3-aminopyrazole in the same manner as in Example 95.

MP:202°C.

MS(EI):479(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 1.65(9H,s), 5.60(1H,s), 7.27-
20 7.41(3H,m), 7.54-7.58(2H,m), 7.64(1H,dd,J=7.3Hz and 7.2Hz), 7.97(1H,d,J=7.3Hz), 8.03(1H,s), 8.10(1H,d,J=7.3Hz), 10.23(1H,brs), 12.26(1H,brs).

Example 335

4-(2,1,3-Benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(indol-3-yl)-2H-pyrazolo[3,4-b]pyridine
25

(1-t-Butoxycarbonylindol-3-yl)-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (0.6 g) was added to trifluoroacetic acid (15 mL) under ice-cooling and the mixture was stirred for 3 hours. The solvent was evaporated under reduced pressure,
30 and ethyl acetate and a saturated aqueous sodium hydrogencarbonate solution were added to neutralize the mixture. The mixture was extracted with ethyl acetate and the solvent was evaporated under reduced pressure. The residue was

recrystallized from ethyl acetate to give the title compound (0.4 g) as colorless crystals.

MP:238°C.

Anal. Calcd. for: $C_{21}H_{13}N_7O \cdot 3/5 H_2O$: C, 64.64; H, 3.67; N, 25.13.

5 Found: C, 64.77; H, 4.05; N, 25.59.

MS(EI): 379 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 5.56(1H, s), 7.08(1H, dd, J=7.3Hz and 7.2Hz), 7.15(1H, dd, J=7.3Hz and 7.2Hz), 7.44(1H, s), 7.44-7.54(3H, m), 7.65(1H, dd, J=7.3Hz and 7.2Hz), 7.76(1H, s),
10 7.95(1H, d, J=7.3Hz), 9.98(1H, brs), 11.63(1H, brs), 12.20(1H, brs).

Example 336

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-3-dimethoxymethyl-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
15 dimethylacetate, methyl butyrate and 2-chlorobenzaldehyde in the same manner as in Example 302.

MP:212°C.

Anal. Calcd. for: $C_{19}H_{21}ClN_4O_2$: C, 61.21; H, 5.68; N, 15.03.

Found: C, 61.25; H, 5.69; N, 15.17.

20 MS(EI): 372 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.88(3H, t, J=7.3Hz), 1.57-1.63(2H, m), 2.28-2.35(2H, m), 2.93(6H, s), 4.93(1H, s), 5.30(1H, s), 7.10(1H, d, J=7.3Hz), 7.19(1H, dd, J=7.3Hz and 7.2Hz), 7.25(1H, dd, J=7.3Hz and 7.2Hz), 7.35(1H, d, J=7.3Hz),
25 9.80(1H, brs), 12.29(1H, brs).

Example 337

5-Cyano-4,7-dihydro-6-propyl-4-(pyridin-4-yl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate,
30 pyridine-4-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:224°C.

Anal. Calcd. for: $C_{15}H_{15}N_5$: C, 67.90; H, 5.70; N, 26.40.

Found: C, 67.90; H, 5.79; N, 26.31.

MS(EI): 265(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.92(3H, t, J=7.3Hz), 1.62-
1.67(2H, m), 2.35-2.43(2H, m), 4.95(1H, s), 7.20(2H, dd, J=4.6Hz
5 and 1.5Hz), 7.29(1H, s), 8.50(2H, dd, J=4.6Hz and 1.5Hz),
9.84(1H, brs), 12.20(1H, brs).

Example 338

5-Cyano-4,7-dihydro-4-(3-methyl-2-nitrophenyl)-6-propyl-2H-
pyrazolo[3,4-b]pyridine

10 The title compound was prepared from methyl butyrate, 3-
methyl-2-nitrobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: 250°C.

Anal. Calcd. for: C₁₇H₁₇N₅O₂: C, 63.15; H, 5.30; N, 21.66.

15 Found: C, 62.89; H, 5.51; N, 22.11.

MS(EI): 323(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.94(3H, t, J=7.3Hz), 1.63-
1.68(2H, m), 2.26(3H, s), 2.36-2.42(2H, m), 4.83(1H, s),
7.17(1H, s), 7.20(1H, d, J=7.3Hz), 7.32(1H, d, J=7.3Hz),
20 7.48(1H, dd, J=7.3Hz and 7.2Hz), 9.91(1H, brs), 12.22(1H, brs).

Example 339

5-Cyano-4,7-dihydro-4-(3-methyl-2-nitrophenyl)-6-isopropyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
25 3-methyl-2-nitrobenzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP: 261°C.

Anal. Calcd. for: C₁₇H₁₇N₅O₂ 1/2 H₂O: C, 61.43; H, 5.46; N, 21.07.

Found: C, 61.82; H, 5.32; N, 21.31.

30 MS(EI): 323(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 1.21(3H, d, J=7.2Hz),
1.26(3H, d, J=7.2Hz), 2.25(3H, s), 3.01(1H, t, J=7.2Hz), 4.84(1H, s),
7.17(1H, s), 7.22(1H, d, J=7.3Hz), 7.32(1H, d, J=7.3Hz),

7.48(1H,dd,J=7.3Hz and 7.2Hz), 9.71(1H,brs), 12.24(1H,brs).

Example 340

5-Cyano-6-cyclopropyl-4,7-dihydro-4-(3-methyl-2-nitrophenyl)-2H-pyrazolo[3,4-b]pyridine

5 The title compound was prepared from methyl cyclopropanecarboxylate, 3-methyl-2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:265°C.

Anal. Calcd. for: C₁₇H₁₅N₅O₂: C, 63.54; H, 4.71; N, 21.79.

10 Found: C, 63.44; H, 4.85; N, 22.04.

MS(EI): 321(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.90-1.07(4H,m), 1.96-

1.99(1H,m), 2.26(3H,s), 4.81(1H,s), 7.17(1H,s),

7.20(1H,d,J=7.3Hz), 7.32(1H,d,J=7.3Hz), 7.48(1H,dd,J=7.3Hz and

15 7.2Hz), 9.23(1H,brs), 12.23(1H,brs).

Example 341

Ethyl 4-(2,1,3-benzoxazol-4-yl)-4,7-dihydro-6-(1-methylethyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate 1/2 ethyl acetate

20 The title compound was prepared from 2,1,3-benzoxazole-4-aldehyde, 3-aminopyrazole and ethyl isobutyrylacetate in the same manner as in Example 275.

MP:190-193°C (decomposition)

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.7.3(3H,t,J=7.1Hz),

1.19(3H,d,J=7.1Hz), 1.29(3H,d,J=7.1Hz), 3.77(2H,m), 4.37(1H,m),

25 5.69(1H,s), 7.12(1H,d,J=6.6Hz), 7.22(1H,s),

7.51(1H,dd,J=6.6,9.0Hz), 7.78(1H,d,J=8.8Hz), 9.31(1H,brs),

12.02(1H,brs).

Example 342

Ethyl 4-(2-nitrophenyl)-4,7-dihydro-6-(1-methylethyl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

30 The title compound was prepared from 2-nitrobenzaldehyde, 3-aminopyrazole and ethyl isobutyrylacetate in the same manner as in Example 275.

MP:205-206°C.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.78(3H,t,J=6.8Hz),
1.15(3H,d,J=7.1Hz), 1.26(3H,d,J=7.1Hz), 3.71(2H,m), 4.33(1H,m),
5.44(1H,s), 7.29-7.34(3H,m), 7.58(1H,m), 7.78(1H,d,J=8.0Hz),
5 9.33(1H,brs), 12.11(1H,brs).

Example 343

Ethyl 4-(2-methoxyphenyl)-4,7-dihydro-6-(1-methylethyl)-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate 1/2 ethyl acetate

The title compound was prepared from 2-
10 methoxybenzaldehyde, 3-aminopyrazole and ethyl
isobutyrylacetate in the same manner as in Example 275.

MP:179-180°C.

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.81(3H,t,J=7.1Hz),
1.17(3H,d,J=7.1Hz), 1.27(3H,d,J=7.1Hz), 3.76(2H,m), 3.85(3H,s),
15 4.31(1H,m), 5.46(1H,s), 6.77(1H,m), 6.89(1H,d,J=8.0Hz),
6.94(1H,d,J=7.6Hz), 7.04(1H,m), 7.14(1H,s), 8.98(1H,brs),
11.86(1H,brs).

Example 344

Ethyl 4-(2-bromophenyl)-4,7-dihydro-6-cyclopropyl-2H-
20 pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from
cyclopropanecarbonyl chloride, 2-bromobenzaldehyde and 3-
aminopyrazole in the same manner as in Example 277.

MP:168-170°C

25 ¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.86(3H,t,J=7.1Hz), 0.87-
0.90(2H,m), 1.10-1.14(2H,m), 3.16(1H,m), 3.78(2H,m),
5.57(1H,s), 7.01(1H,dd,J=5.8,7.6Hz), 7.09(1H,d,J=7.8Hz),
7.24(1H,m), 7.29(1H,s), 7.51(1H,d,J=6.8Hz), 8.65(1H,brs),
12.01(1H,brs).

30 **Example 345**

Ethyl 4-(2-bromo3-cyanophenyl)-4,7-dihydro-6-cyclopropyl-2H-
pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from

cyclopropanecarbonyl chloride, 2-bromo-3-cyanobenzaldehyde and 3-aminopyrazole in the same manner as in Example 277.

MP: 168–170°C

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.86(3H, t, J=7.1Hz), 0.88–
5 1.00(2H, m), 1.10–1.18(2H, m), 3.14(1H, m), 3.80(2H, m),
5.64(1H, s), 7.33(1H, s), 7.34–7.49(2H, m), 7.68(1H, m),
8.77(1H, brs), 12.10(1H, brs).

Example 346

4-(2-Chlorophenyl)-5-cyano-7-methyl-6-propyl-4,7-dihydro-2H-
10 pyrazolo[3,4-b]pyridine

A solution of 3-aminopyrazole (3.0 g), di-t-butyl dicarbonate (17.3 g) and dimethylaminopyridine (1.3 g) in tetrahydrofuran (360 ml) was stirred at room temperature. The reaction mixture was concentrated under reduced pressure. The
15 obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to give a mixture (7.9 g) of 1-(t-butoxycarbonyl)-3-(t-butoxycarbonylamino)pyrazole and 2-(t-butoxycarbonyl)-3-(t-butoxycarbonylamino)pyrazole as a white amorphous solid. To a
20 suspension of the obtained white amorphous solid (7.9 g) and sodium hydride (1.1 g) in DMF (80 ml) was added methyl iodide (4.0 g) under ice-cooling and the mixture was stirred at room temperature for 1 hour. To the reaction mixture was added water under ice-cooling and the resulting mixture was
25 extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure. The obtained residue was purified by silica gel column chromatography (eluent: hexane-ethyl acetate (10:1)) to
30 give a white solid (5.3 g). The obtained white solid (5.3 g) was dissolved in methylene chloride (50 ml), and trifluoroacetic acid (7 ml) was added. The resulting mixture was stirred at room temperature for 20 hours. The reaction

mixture was concentrated under reduced pressure and the obtained residue was purified by silica gel column chromatography (eluent: chloroform-methanol (10:1)) to give 3-methylaminopyrazole (1.54 g) as a colorless transparent oil.

- 5 Subsequently, the title compound was prepared from methyl butyrate, 2-chlorobenzaldehyde and 3-methylaminopyrazole in the same manner as in Example 94.

MP:170-171°C

Anal. Calcd. for: $C_{17}H_{17}N_4Cl$: C, 65.28; H, 5.48; N, 17.91.

- 10 Found: C, 65.14; H, 5.52; N, 17.72.

MS(EI): 312 (M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 1.00 (3H, t, $J=7.3$ Hz), 1.68 (2H, m), 2.62 (2H, m), 3.36 (3H, s), 5.36 (1H, s), 7.22-7.26 (2H, m), 7.30-7.32 (2H, m), 7.42 (1H, d, $J=8.1$ Hz), 12.31 (1H, brs).

- 15 **Example 347**

4-(2,1,3-Benzoxazol-4-yl)-5-cyano-7-methyl-6-propyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

- The title compound was prepared from methyl butyrate, 2,1,3-benzoxazole-4-aldehyde and 3-methylaminopyrazole in the same manner as in Example 346.

MP:198-200°C

Anal. Calcd. for: $C_{17}H_{16}N_6O$: C, 63.74; H, 5.03; N, 26.23.

Found: C, 63.78; H, 5.12; N, 26.47.

MS(EI): 320 (M^+).

- 25 1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.97 (3H, t, $J=7.4$ Hz), 1.61 (2H, m), 2.63 (2H, m), 3.41 (3H, s), 5.40 (1H, s), 7.32 (1H, s), 7.40 (1H, d, $J=6.6$ Hz), 7.59 (1H, dd, $J=6.5, 6.6$ Hz), 7.92 (1H, d, $J=9.3$ Hz), 12.30 (1H, brs).

Example 348

- 30 4-(2-Bromo-3-cyanophenyl)-5-cyano-7-methyl-6-propyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 2-bromo-3-cyanobenzaldehyde and 3-methylaminopyrazole in the

same manner as in Example 346.

MP:218-220°C

Anal. Calcd. for: C₁₈H₁₆N₅Br: C, 56.56; H, 4.22; N, 18.32.

Found: C, 56.60; H, 4.41; N, 18.18.

5 MS(EI): 382(M⁺).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 1.00(3H, t, J=7.3Hz), 1.63(2H, m),
2.62(2H, m), 3.37(3H, s), 5.47(1H, s), 7.39(1H, s), 7.56-
7.58(2H, m), 7.83(1H, m), 12.41(1H, brs).

Example 349

10 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-
pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl acetate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

15 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 2.14(3H, s), 5.35(1H, s), 7.21-
7.33(4H, m), 7.42(1H, d, J=8.1Hz), 9.87(1H, brs), 12.15(1H, brs).

Example 350

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(morpholin-4-
yl)methyl-2H-pyrazolo[3,4-b]pyridine dihydrochloride

20 A solution of 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine (22.9 g), di-t-butyl dicarbonate (19.4 g) and dimethylaminopyridine (0.5 g) in tetrahydrofuran (200 ml) was stirred at room temperature for 30 minutes. The reaction mixture was ice-cooled and the
25 precipitated crystals were collected by filtration to give 2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine (21.8 g) as white crystals.
2-(t-Butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-methyl-2H-pyrazolo[3,4-b]pyridine (5.0 g), N-bromosuccinimide
30 (2.5 g) and azobisisobutyronitrile (66 mg) were suspended in benzene (50 ml) and the suspension was stirred for 1 hour. The reaction mixture was concentrated under reduced pressure, and the obtained residue was purified by silica gel column

chromatography (eluent: hexane-ethyl acetate (2:1)) and crystallized from ethyl acetate to give 6-bromomethyl-2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine as white crystals. To a suspension of
5 sodium hydride (32 mg) in DMF (10 ml) was added morpholine (70 µl) and the mixture was stirred at room temperature for 30 minutes. To the reaction mixture was added 6-bromomethyl-2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (0.36 g) and the mixture was stirred
10 under ice-cooling for 1 hour. To the reaction mixture was added water, and the precipitated crystals were collected by filtration and washed with hexane to give 2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-(morpholin-4-yl)methyl-2H-pyrazolo[3,4-b]pyridine (450 mg) as
15 white crystals. A solution of 2-(t-butoxycarbonyl)-4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-(morpholin-4-yl)methyl-2H-pyrazolo[3,4-b]pyridine (440 mg) in trifluoroacetic acid (5 ml) was stirred at room temperature for 30 minutes. The reaction mixture was concentrated under reduced pressure and
20 4M hydrochloric acid-dioxane solution was added. The precipitated crystals were collected by filtration and washed with ethyl acetate to give the title compound (250 mg) as pale-yellow crystals.

MP:210-214°C (decomposition).

25 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 3.20-3.40(3H,m), 3.84-4.00(3H,m), 4.17-4.40(4H,m), 5.49(1H,s), 7.26-7.37(4H,s), 7.45(1H,d,J=7.8Hz), 10.22(1H,brs), 11.05(1H,brs), 12.33(1H,brs).

Example 351

30 6-Benzylloxymethyl-4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from ethyl benzyloxyacetate, 2-chlorobenzaldehyde and 3-aminopyrazole in

the same manner as in Example 94.

MP:165-166°C

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 4.35(2H, d, J=2.9Hz), 4.57(2H, s), 5.42(1H, s), 7.24-7.45(10H, m), 10.03(1H, brs), 12.22(1H, brs).

5 **Example 352**

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(methylpiperazin-1-yl)methyl-2H-pyrazolo[3,4-b]pyridine dihydrochloride

4-(2-Chlorophenyl)-5-cyano-6-(t-butyldimethylsilyloxy)-methyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine was prepared
10 from ethyl t-butyldimethylsilyloxyacetate, 2-chlorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94. To a solution of 4-(2-chlorophenyl)-5-cyano-6-(t-butyldimethylsilyloxy)methyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (10 g) in tetrahydrofuran (100 ml) was added a THF
15 solution (24.9 ml) of 1.0 M tetrabutylammonium fluoride and the mixture was stirred at room temperature for 1 hour. To the reaction mixture was added ethyl acetate (200 ml), and the resulting mixture was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate.
20 The solvent was evaporated and the obtained residue was crystallized from ethyl acetate to give 4-(2-chlorophenyl)-5-cyano-6-hydroxymethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (5.46 g) as a white solid. To a solution of 4-(2-chlorophenyl)-5-cyano-6-hydroxymethyl-4,7-dihydro-2H-
25 pyrazolo[3,4-b]pyridine (1.0 g) and carbon tetrabromide (1.27 g) in methylene chloride (35 ml) was added triphenylphosphine (1.0 g) under ice-cooling and the mixture was stirred under ice-cooling for 4 hours. The reaction mixture was concentrated under reduced pressure and the obtained residue was purified
30 by silica gel column chromatography (eluent: hexane-ethyl acetate (1:1)) to give 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (0.45 g) as a pale-yellow solid. To a suspension of sodium hydride (25 mg)

in DMF (3 ml) was added 1-methylpiperazine (69 μ l) and the mixture was stirred at room temperature for 30 minutes. To this reaction mixture was added a solution of 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine (200 mg) in DMF (3 ml) under ice-cooling and the mixture was stirred under ice-cooling for 1 hour. To the reaction mixture was added water and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (eluent: ethyl acetate-methanol (4:1)). The obtained oil was treated with hydrogen chloride-methanol to give the title compound (87 mg) as white crystals.

MP:222-225°C (decomposition)

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 2.66-2.75(2H,m), 2.75(3H,s), 3.00-3.10(4H,m), 3.41-3.55(4H,m), 5.42(1H,s), 7.24-7.36(4H,m), 7.43(1H,d,J=8.0Hz), 9.77(1H,brs), 12.17(1H,brs).

Example 353

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-6-(piperidin-1-yl)methyl-2H-pyrazolo[3,4-b]pyridine hydrochloride

The title compound was prepared from 4-(2-chlorophenyl)-5-cyano-6-bromomethyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine and piperidine in the same manner as in Example 352.

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 1.43(1H,m), 1.67-1.82(5H,m), 3.05-3.25(2H,m), 3.48(2H,m), 4.10(2H,m), 5.49(1H,s), 7.26-7.35(4H,m), 7.45(1H,d,J=8.0Hz), 10.28(1H,brs), 10.59(1H,brs).

Example 354

Ethyl 4-(2-nitrophenyl)-4,7-dihydro-6-cyclopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from cyclopropanecarbonyl chloride, 2-nitrobenzaldehyde and 3-aminopyrazole in the same manner as in Example 277.

MP:162-164°C (decomposition)

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.81(3H,t,J=7.4Hz), 0.85-
0.95(2H,m), 1.10-1.18(2H,m), 3.12(1H,m), 3.72(2H,m),
5.46(1H,s), 7.27-7.34(3H,m), 7.58(1H,m), 7.78(1H,d,J=8.0Hz),
5 8.78(1H,brs), 12.12(1H,brs).

Example 355

Ethyl 4-(2,1,3-benzoxazol-4-yl)-4,7-dihydro-6-cyclopropyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate

The title compound was prepared from
10 cyclopropanecarbonyl chloride, 2,1,3-benzoxazole-4-aldehyde
and 3-aminopyrazole in the same manner as in Example 277.

MP:109-111°C (decomposition).

¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.76(3H,t,J=6.8Hz), 0.85-
0.86(2H,m), 1.14-1.18(2H,m), 3.12(1H,m), 3.80(2H,m),
15 5.69(1H,s), 7.13(1H,d,J=6.6Hz), 7.23(1H,s), 7.51(1H,m),
7.79(1H,d,J=9.0Hz), 8.83(1H,brs), 12.05(1H,brs).

Example 356

4-(2,1,3-Benzoxazol-4-yl)-5-cyano-4,7-dihydro-2-(phenylcarbamoyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

20 The title compound was obtained as colorless crystals
from 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and phenylisocyanate in the same manner as in Example 204.

MS(EI):425(M⁺).

25 ¹H-NMR (400MHz, DMSO-d₆)δ(ppm): 0.91(3H,t,J=7.3Hz), 1.64(2H,m),
2.58(2H,m), 5.44(1H,s), 7.10(1H,dd,J=6.3 and 7.6Hz), 7.31-
7.34(2H,m), 7.52(1H,d,J=6.6Hz), 7.59-7.64(3H,m), 7.95(1H,s),
7.97(1H,d,J=9.0Hz), 9.83(1H,brs), 10.30(1H,brs).

Example 357

30 4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-1-(4-pentenoyl)-6-propyl-1H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-

pyrazolo[3,4-b]pyridine, dimethylaminopyridine and 4-pentenoyl chloride in the same manner as in Example 204.

MP:140°C.

Anal. Calcd. for: C₂₁H₂₁ClN₄O: C, 66.22; H, 5.62; N, 14.71.

5 Found: C, 66.20; H, 5.60; N, 14.65.

MS(EI): 380(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.95(3H, t, J=7.3Hz), 1.62(2H, m),
2.39-2.58(4H, m), 3.11(2H, t, J=7.6Hz), 4.98(1H, d, J=7.1Hz),
5.06(1H, d, J=10.3Hz), 5.40(1H, s), 5.85(1H, m), 7.27-7.37(4H, m),
10 7.46(1H, d, J=7.0Hz), 9.58(1H, brs).

Example 358

4-(2-Chlorophenyl)-5-cyano-4,7-dihydro-2-(4-pentenoyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was obtained as colorless crystals
15 from 4-(2-chlorophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine, dimethylaminopyridine and 4-pentenoyl chloride in the same manner as in Example 204.

MP:176-177°C.

Anal. Calcd. for: C₂₁H₂₁ClN₄O: C, 66.22; H, 5.56; N, 14.71.

20 Found: C, 66.15; H, 5.63; N, 14.55.

MS(EI): 380(M⁺).

¹H-NMR (400MHz, DMSO-d₆) δ(ppm): 0.95(3H, t, J=7.3Hz), 1.67(2H, m),
2.34-2.49(4H, m), 3.00(2H, t, J=7.6Hz), 4.96(1H, d, J=10.6Hz),
5.02(1H, d, J=27.1Hz), 5.36(1H, s), 5.82(1H, m), 7.30-7.35(3H, m),
25 7.46(1H, d, J=7.8Hz), 7.83(1H, s), 10.39(1H, brs).

Example 359

5-Cyano-4,7-dihydro-4-(6-methylpyridin-2-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 6-
30 methylpyridine-2-aldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:177-181°C.

Anal. Calcd. for: C₁₆H₁₇N₅ 4/5 H₂O: C, 65.42; H, 6.38; N, 23.84.

Found: C, 65.52; H, 6.31; N, 24.19.

MS(EI): 279 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.95(3H, t, $J=7.6\text{Hz}$), 1.66(2H, m),
2.41(2H, m), 2.43(3H, s), 4.94(1H, s), 6.98(1H, d, $J=7.6\text{Hz}$),
5 7.06(1H, d, $J=7.5\text{Hz}$), 7.21(1H, s), 7.62(1H, dd, $J=7.6$ and 7.7Hz),
9.71(1H, brs), 12.09(1H, brs).

Example 360

4-(5-Cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine)pyridine-N-oxide

10 The title compound was prepared from methyl butyrate, pyridine-4-aldehyde-N-oxide and 3-aminopyrazole in the same manner as in Example 94.

MP: 110–115°C.

Anal. Calcd. for: $\text{C}_{15}\text{H}_{15}\text{N}_5\text{O}$: C, 62.01; H, 6.18; N, 24.11.

15 Found: C, 61.94; H, 5.85; N, 23.73.

MS(EI): 283 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, $J=7.3\text{Hz}$), 1.62(2H, m),
2.36(2H, m), 4.98(1H, s), 7.18(2H, d, $J=6.6\text{Hz}$), 7.31(1H, s),
8.14(2H, d, $J=6.3\text{Hz}$), 9.86(1H, brs), 12.2(1H, brs).

20 Example 361

5-Cyano-4,7-dihydro-4-(3-(4-morpholinomethyl)phenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 3-(4-morpholinomethyl)benzaldehyde and 3-aminopyrazole in the
25 same manner as in Example 94.

MS(EI): 363 (M^+).

$^1\text{H-NMR}$ (400MHz, DMSO- d_6) δ (ppm): 0.92(3H, t, $J=7.3\text{Hz}$), 1.63(2H, m),
2.30(4H, m), 2.30(2H, m), 3.40(2H, s), 3.53(4H, m), 4.86(1H, s),
7.05(1H, d, $J=7.8\text{Hz}$), 7.10(1H, d, $J=7.6\text{Hz}$), 7.14(1H, s), 7.19(1H, s),
30 7.23(1H, dd, $J=7.5$ and 7.6Hz), 9.70(1H, brs), 12.10(1H, brs).

Example 362

4-(3-Bromophenyl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 3-bromobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:202-205°C.

5 Anal. Calcd. for: $C_{16}H_{15}BrN_4$: C, 55.99; H, 4.41; N, 16.32.

Found: C, 55.82; H, 4.46; N, 17.03.

MS(EI): 343(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.91(3H, t, J=7.3Hz), 1.63(2H, m),
2.37(2H, m), 4.92(1H, s), 7.18(1H, d, J=7.9Hz), 7.25(1H, s),
10 7.28(1H, d, J=7.8Hz), 7.33(1H, s), 7.39(1H, d, J=8.3Hz),
9.80(1H, brs), 12.18(1H, brs).

Example 363

5-Cyano-4,7-dihydro-4-(4-fluoro-2-chlorophenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

15 The title compound was prepared from methyl butyrate, 2-chloro-4-fluorobenzaldehyde and 3-aminopyrazole in the same manner as in Example 94.

MP:209-212°C.

Anal. Calcd. for: $C_{16}H_{14}ClFN_4$: C, 60.67; H, 4.45; N, 17.69.

20 Found: C, 60.48; H, 4.48; N, 17.87.

MS(EI): 316(M^+).

1H -NMR (400MHz, DMSO- d_6) δ (ppm): 0.93(3H, t, J=7.3Hz), 1.64(2H, m),
2.39(2H, m), 5.33(1H, s), 7.17-7.40(3H, m), 7.41(1H, dd, J=2.7 and
6.1Hz), 9.85(1H, brs), 12.17(1H, brs).

25 Example 364

5-Cyano-4,7-dihydro-4-(3-(morpholin-4-yl)phenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl butyrate, 3-(morpholin-4-yl)benzaldehyde and 3-aminopyrazole in the same
30 manner as in Example 94.

MP:196-200°C.

Anal. Calcd. for: $C_{20}H_{23}N_5O$: C, 68.47; H, 6.63; N, 20.04.

Found: C, 68.41; H, 6.77; N, 20.16.

MS(EI):349(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.92(3H,t,J=7.3Hz), 1.63(2H,m),
2.32(2H,m), 3.05(4H,t,J=4.6Hz), 7.71(4H,t,J=4.6Hz), 4.80(1H,s),
6.59(1H,d,J=7.5Hz), 6.74(1H,m), 6.76(1H,s), 7.13(1H,dd,J=7.8
5 and 7.8Hz), 7.21(1H,s), 9.67(1H,brs), 12.02(1H,brs).

Example 365

5-Cyano-4,7-dihydro-4-(3-(morpholin-4-yl)phenyl)-6-isopropyl-
2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl isobutyrate,
10 3-(morpholin-4-yl)benzaldehyde and 3-aminopyrazole in the same
manner as in Example 94.

MP:254-257°C.

Anal. Calcd. for:C₂₀H₂₃N₅O:C,68.47;H,6.63;N,20.04.

Found:C,68.56;H,6.73;N,20.30.

15 MS(EI):349(M⁺).

¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 1.20(3H,d,J=7.0Hz),
1.22(3H,d,J=7.1Hz), 3.02(2H,m), 3.04(4H,t,J=4.8Hz),
3.70(4H,t,J=4.8Hz), 4.78(1H,s), 6.59(1H,d,J=7.6Hz), 7.74(1H,s),
7.13(1H,dd,J=7.5 and 8.1Hz), 7.22(1H,s), 9.48(1H,brs),
20 12.09(1H,brs).

Example 366

5-Cyano-6-cyclopropyl-4,7-dihydro-4-(3-(morpholin-4-
yl)phenyl)-2H-pyrazolo[3,4-b]pyridine

The title compound was prepared from methyl
25 cyclopropanecarboxylate, 3-(morpholin-4-yl)benzaldehyde and 3-
aminopyrazole in the same manner as in Example 94.

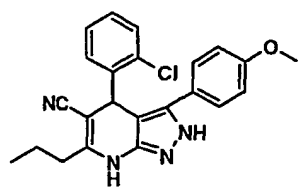
MP:>260°C.

MS(EI):347(M⁺).

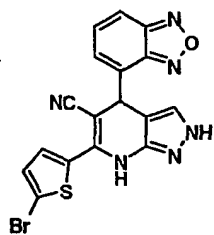
¹H-NMR (400MHz,DMSO-d₆)δ(ppm): 0.86(4H,m), 1.93-1.98(1H,m),
30 3.05(4H,t,J=4.6Hz), 3.70(4H,t,J=4.6Hz), 4.79(1H,s),
6.56(1H,d,J=7.5Hz), 6.74(1H,s), 6.77(1H,s), 7.13(1H,dd,J=7.8
and 7.8Hz), 7.20(1H,s), 8.98(1H,brs),12.09(1H,brs).

The compounds of the above-described Examples are as

follows.



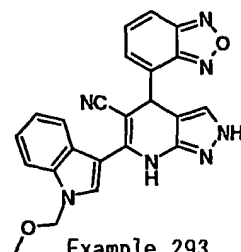
Example 290



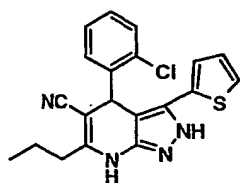
Example 291



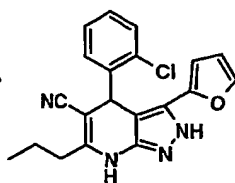
Example 292



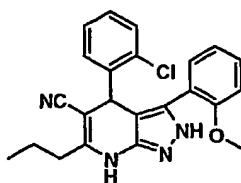
Example 293



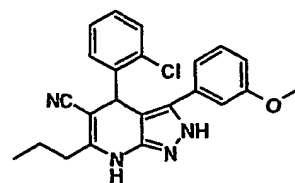
Example 294



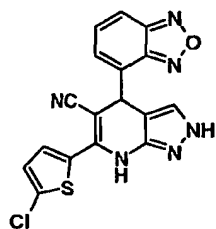
Example 295



Example 296



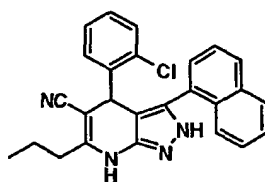
Example 297



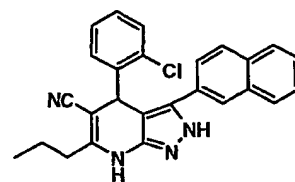
Example 298



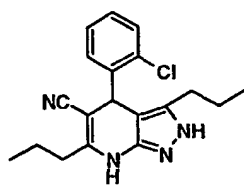
Example 299



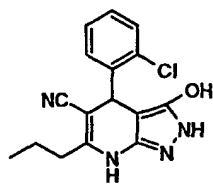
Example 300



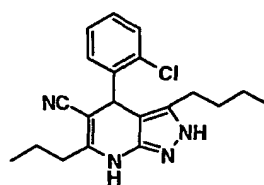
Example 301



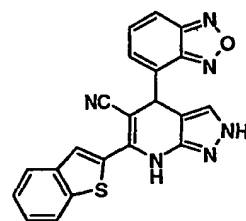
Example 302



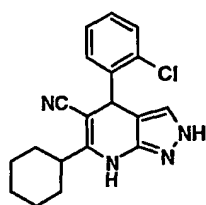
Example 303



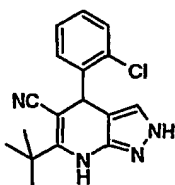
Example 304



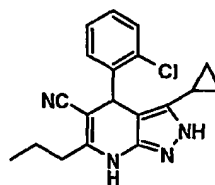
Example 305



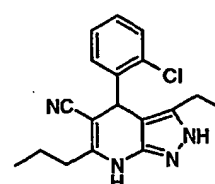
Example 306



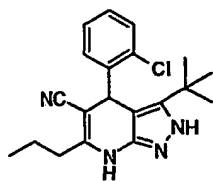
Example 307



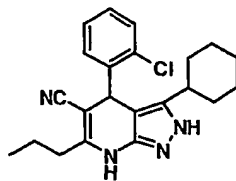
Example 308



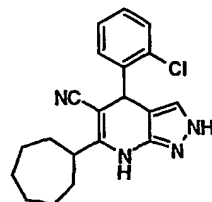
Example 309



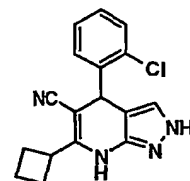
Example 310



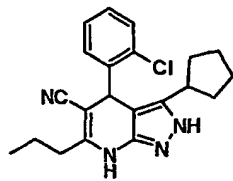
Example 311



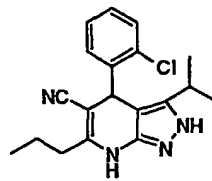
Example 312



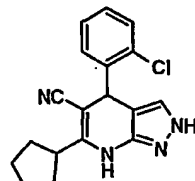
Example 313



Example 314



Example 315



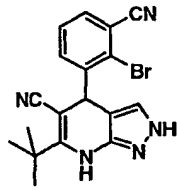
Example 316



Example 317



Example 318



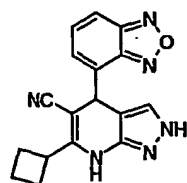
Example 319



Example 320



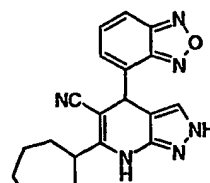
Example 321



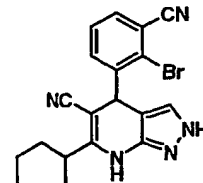
Example 322



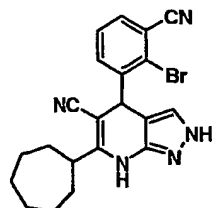
Example 323



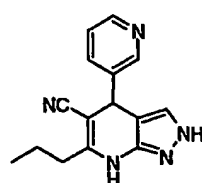
Example 324



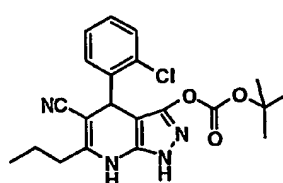
Example 325



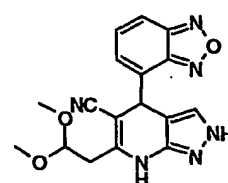
Example 326



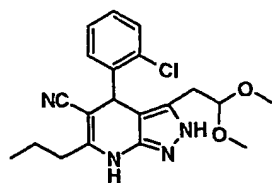
Example 327



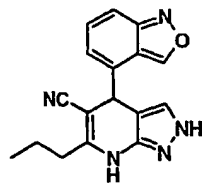
Example 328



Example 329



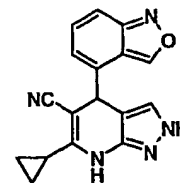
Example 330



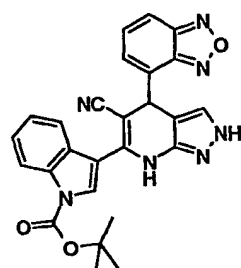
Example 331



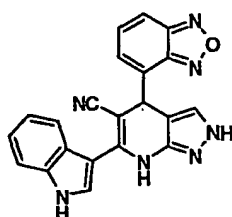
Example 332



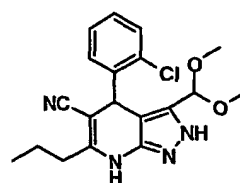
Example 333



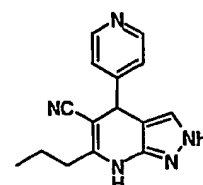
Example 334



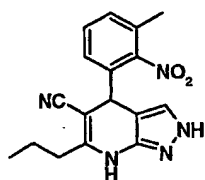
Example 335



Example 336



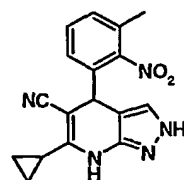
Example 337



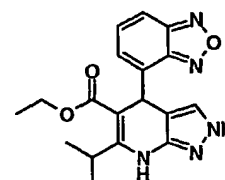
Example 338



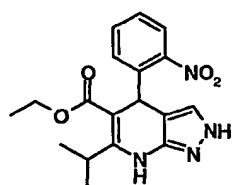
Example 339



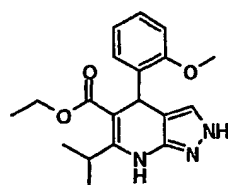
Example 340



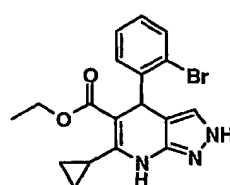
Example 341



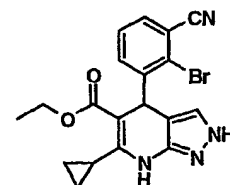
Example 342



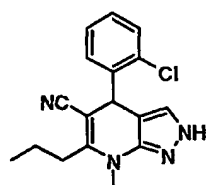
Example 343



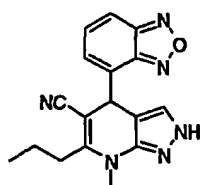
Example 344



Example 345



Example 346



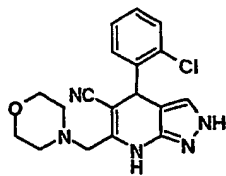
Example 347



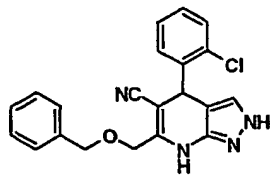
Example 348



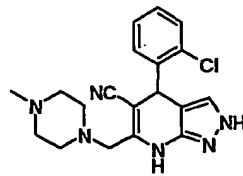
Example 349



Example 350



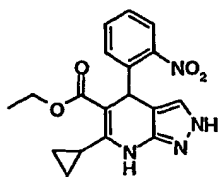
Example 351



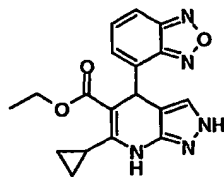
Example 352



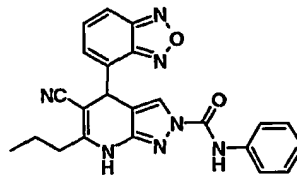
Example 353



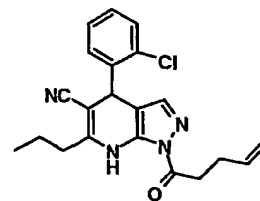
Example 354



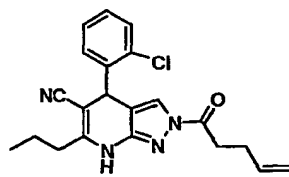
Example 355



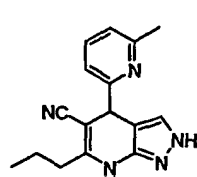
Example 356



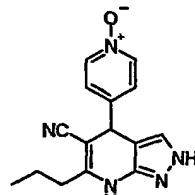
Example 357



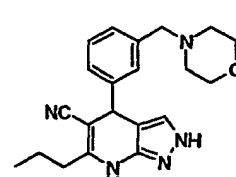
Example 358



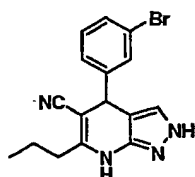
Example 359



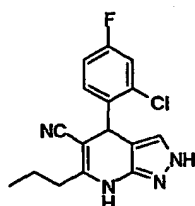
Example 360



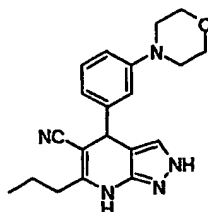
Example 361



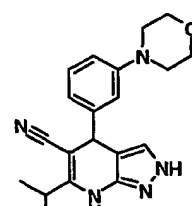
Example 362



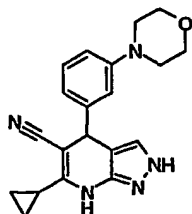
Example 363



Example 364



Example 365



Example 366

Formulation Example 1

The compound of Example 1 (0.5 part), lactose (25 parts), crystalline cellulose (35 parts) and corn starch (3 parts) were thoroughly mixed and kneaded well with a binder made of
5 corn starch (2 parts). The kneaded product was passed through a 16 mesh sieve, dried in an oven at 50°C and passed through a 4 mesh sieve. The kneaded powder thus obtained, corn starch (8 parts), crystalline cellulose (11 parts) and talc (9 parts) were thoroughly mixed and compression-punched to give tablets
10 containing 0.5 mg of the active ingredient per tablet.

Formulation Example 2

The compound of Example 1 (1.0 mg) and sodium chloride (9.0 mg) were dissolved in water for injection and the solution was filtered to remove pyrogen. The filtrate was
15 transferred into ampoules under sterile conditions. After sterilization, the ampoules were weld-sealed to give injections each containing 1.0 mg of the active ingredient.

The effects of the compounds of the present invention on glycogen synthase kinase-3 beta (GSK-3 β) were evaluated and
20 confirmed as follows.

Experimental Example 1: GSK-3 β -inhibitory activity

CREB phosphopeptide (4.6 nmol), rabbit GSK-3 β (0.5 unit), ATP (5 nmol), [γ -³²P]ATP (12.3 kBq) and a test compound were reacted in a GSK-3 β buffer solution (25 μ L) (20 mmol/L Tris-HCl
25 (pH 7.5), 10 mmol/L magnesium chloride, 5 mmol/L dithiothreitol) containing 1% dimethyl sulfoxide, at 30°C for 20 minutes. The reaction product (10 μ L) was adsorbed on a P81 ion-exchange paper, and the paper was washed with phosphoric acid (100 mmol/L) and measured for cpm on a scintillation
30 counter. As a result, the compounds of the present invention showed the IC₅₀ values of 1 to 1000 nmol/L. For example, the IC₅₀ values of the compounds of Examples 1, 14, 27, 66 and 140 were 210, 170, 25, 51 and 24 nmol/L, respectively.

CREB Phosphopeptide is Lys-Arg-Arg-Glu-Ile-Leu-Ser-Arg-Arg-Pro-Ser(P)-Tyr-Arg.

Experimental Example 2: GSK-3 β -inhibitory activity in rat cultured hippocampal neurons

5 Hippocampal neurons were obtained from rat embryos on the 18th day after conception. After culturing the hippocampal neurons for 7 days, the neurons were treated with amyloid β (25-35) (20 μ mol/L) and a test compound (GSK-3 β inhibitor) and the culture was continued for 3 hours, whereby phosphorylation
10 of Tau protein was induced. After the completion of culture, the level of phosphorylation of Tau protein was determined by EIA method using phosphorylated Tau-recognizing antibody (phosphorylated site by GSK-3 β) and the inhibitory effect of the GSK-3 β inhibitor on the neurons was evaluated. Fig. 1
15 shows the GSK-3 β -inhibitory activity of the compounds of Example 47 and Example 137.

Experimental Example 3: Effect on amyloid β -induced cytotoxicity in rat cultured hippocampal neurons

Hippocampal neurons were obtained from rat embryos on
20 the 18th day after conception. After culturing the hippocampal neurons for 7 days, the neurons were treated with amyloid β (25-35) (20 μ mol/L) and a test compound (GSK-3 β inhibitor) and the culture was continued for 24 hours, whereby cytotoxicity (decreased activity of intracellular dehydrogenases) was
25 induced. After the completion of culture, activity of intracellular dehydrogenases was determined and the effect of the GSK-3 β inhibitor on the amyloid β -induced cytotoxicity was evaluated. Fig. 2 shows the effect of the compounds of Example 66 on amyloid β -induced cytotoxicity.

30 **Experimental Example 4: GSK-3 β -inhibitory effect in gerbil brain ischemia model**

A test compound (GSK-3 β inhibitor) was intraperitoneally administered to gerbils and 30 minutes later, brain ischemia

was created by shutting off (for 4 minutes) all carotid arteries, whereby phosphorylation of Tau protein in the brain was induced. Three hours after the brain ischemia, the hippocampus was obtained from the gerbil brain and the level
5 of phosphorylation of Tau protein was determined by Western blot using phosphorylated Tau-recognizing antibody (phosphorylated site by GSK-3 β), based on which the GSK-3 β -inhibitory effect of the GSK-3 β inhibitor in the gerbil brain was evaluated. Fig. 3 shows the GSK-3 β -inhibitory effect of
10 the compounds of Example 27 in gerbil brain ischemia model.

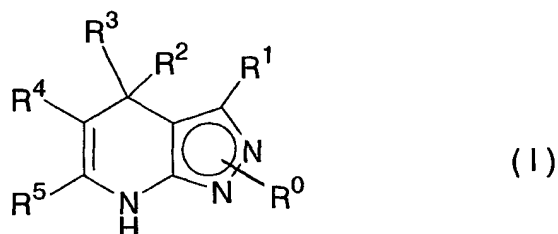
Industrial Applicability

The compounds of the present invention show a selective and strong inhibitory action on glycogen synthase kinase-3
15 beta (GSK-3 β), and are useful as medicaments for prevention and/or treatment of diabetes, diabetic complications and neurodegenerative diseases (Alzheimer's disease, ischemic cerebrovascular disorder, Down's syndrome, cerebral ischemia due to cerebral amyloid angiopathy, progressive supranuclear
20 paralysis, subacute sclerosing panencephalitic Parkinsonism, postencephalitic Parkinsonism, boxer's encephalopathy, Parkinson dementia complex of Guam, Lewy body disease, Pick's disease, corticobasal degeneration, frontotemporal dementia, AIDS encephalopathy, Huntington's disease, manic-depressive
25 psychosis and the like), or as immunopotentiators.

This application is based on patent application Nos. 2001-304707, 2001-26379 and 2001-081238 filed in Japan, the contents of which are hereby incorporated by reference.

CLAIMS

1. A dihydropyrazolopyridine compound of the formula (I):



5

wherein

R⁰ is hydrogen, alkyl, acyl, cycloalkyl, formyl, haloalkyl, aminoalkyl, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, aminocarbonyl, alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, acyloxyacetyl, acyloxyalkyl, phenyl optionally having substituent(s), aromatic heterocyclic group optionally having substituent(s), phenylalkyl optionally having substituent(s), or a group of the formula: -COOR⁸ (wherein R⁸ is hydrogen, alkyl, aryl optionally having substituent(s) or aralkyl optionally having substituent(s));

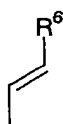
R¹ and R² are the same or different and each is hydrogen, alkyl, acyl, cycloalkyl, hydroxy, thiol, halogen, amino, formyl, carboxy, cyano, nitro, alkylthio, haloalkyl, aminoalkyl, acylamino, alkoxy, cycloalkoxy, phenoxy, phenylalkoxy, aminoalkoxy, alkoxyalkyl, phenoxyalkyl, hydroxyalkyl, alkoxycarbonyl, aminocarbonyl, alkylthiocarbonyl, carboxyalkyl, cycloalkoxyalkyl, phenylthio, alkylsulfinyl, alkylsulfonyl, phenylsulfonyl, mercaptoalkyl, alkylthioalkyl, phenyl optionally having substituent(s), aromatic heterocyclic group or phenylalkyl;

25

20

R³ is

- (1) alkyl or haloalkyl,
- (2) cycloalkyl,
- (3) phenyl optionally having substituent(s),
- 5 (4) aromatic heterocyclic group,
- (5) a group derived from a benzene ring fused with a saturated or unsaturated 5 or 6 membered carbocyclic ring,
- (6) a group derived from a benzene ring fused with a saturated or unsaturated 5 to 7 membered carbocyclic ring containing 1 to 3 heteroatom(s), or
- 10 (7) a group derived from a 5 to 7 membered saturated or unsaturated carbocyclic ring containing 1 to 3 heteroatom(s), which is fused with a benzene ring,
- 15 wherein the groups of (2) to (7) may have one or more substituent(s), or
- a group selected from the groups represented by the following formulas (II) and (III),



(II)



(III)

wherein R⁶ and R⁷ are each phenyl optionally having substituent(s) or an aromatic heterocyclic group,
 or R² and R³ in conjunction form a ring optionally containing
 25 heteroatom(s), wherein the ring may be fused with a benzene ring optionally having substituent(s);
 R⁴ is alkoxy carbonyl, aminocarbonyl, hydrazinocarbonyl, alkylthiocarbonyl, formyl, carbamoyl, alkylthio, phenylthio, alkylsulfinyl, phenylsulfinyl,

alkylsulfonyl, phenylsulfonyl, dialkylphosphinyl,
dialkylphosphonyl, cyano or nitro; and
R⁵ is hydrogen, cyano, formyl, alkyl, cycloalkyl,
alkoxyalkyl, phenoxyalkyl, dialkoxyalkyl,
5 hydroxyalkyl, haloalkyl, carboxyalkyl,
cycloalkoxyalkyl, phenylthio, alkylsulfinyl,
alkylsulfonyl, phenylsulfonyl, mercaptoalkyl,
alkylthioalkyl, alkoxycarbonylalkyl,
alkoxycarbonylethenyl, aryl optionally having
10 substituent(s), an aromatic heterocyclic group or
phenylalkyl, or a group derived from a 5 to 7
membered saturated or unsaturated carbocyclic ring
containing 1 to 3 heteroatom(s), which is fused with
a benzene ring,
15 or R⁴ and R⁵ in conjunction may form a 5 or 6 membered ring
optionally containing heteroatom(s),
provided that when R⁰, R¹ and R² are each hydrogen, R⁴ is
methoxycarbonyl and R⁵ is methyl, then R³ should not
be phenyl, 2-chlorophenyl, 3-nitrophenyl, 4-
20 carboxyphenyl or 4-methoxycarbonylphenyl,
or an optically active form thereof, a pharmaceutically
acceptable salt thereof or a hydrate thereof.

2. The dihydropyrazolopyridine compound of claim 1, wherein R⁵
25 is alkyl having 2 to 8 carbon atoms, cycloalkyl, alkoxyalkyl,
phenoxyalkyl, hydroxyalkyl, phenyl optionally having
substituent(s), an aromatic heterocyclic group or phenylalkyl,
or an optically active form thereof, a pharmaceutically
acceptable salt thereof or a hydrate thereof.

30 3. The dihydropyrazolopyridine compound of claim 1, wherein R¹
is hydrogen, alkyl, phenyl optionally having substituent(s),
an aromatic heterocyclic group or phenylalkyl, or an optically

active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

4. The dihydropyrazolopyridine compound of claim 1, wherein R²
5 is hydrogen or alkyl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

5. The dihydropyrazolopyridine compound of claim 1, wherein R³
is phenyl optionally having 1 to 3 substituent(s), naphthyl,
10 2,1,3-benzoxadiazol-4-yl or 3,4-dihydro-2H-benzopyran-8-yl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

6. The dihydropyrazolopyridine compound of claim 1, wherein R⁴
15 is alkoxycarbonyl having 2 to 5 carbon atoms, cyano or nitro, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

7. The dihydropyrazolopyridine compound of claim 1, wherein R⁵
20 is alkyl having 2 to 4 carbon atoms, cyclopropyl, phenyl, thienyl or hydroxyalkyl, or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

8. The dihydropyrazolopyridine compound of claim 1, wherein R²
25 and R³ in conjunction form a ring containing sulfur atom and the ring is condensed with a benzene ring optionally having substituent(s), or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

30

9. The dihydropyrazolopyridine compound of claim 1, wherein R⁰
is hydrogen or a group of the formula: -COOR⁸ (wherein R⁸ is alkyl, aryl optionally having substituent(s) or aralkyl

optionally having substituent(s)), or an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

- 5 10. The dihydropyrazolopyridine compound of claim 1, which is selected from the group consisting of
- (32) ethyl 4,7-dihydro-4-(2-methoxyphenyl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (47) ethyl 4-(2-chloro-3-trifluoromethylphenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- 10 (66) ethyl 4,7-dihydro-4-(naphthalen-1-yl)-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (73) ethyl 4-(3,4-dihydro-2H-benzopyran-8-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- 15 (87) ethyl 4-(2-chlorophenyl)-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (116) ethyl 4-(2,1,3-benzoxadiazol-4-yl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (122) 4-(2,3-dichlorophenyl)-4,7-dihydro-5-nitro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
- 20 (140) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine,
- (147) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine,
- 25 (158) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-phenyl-2H-pyrazolo[3,4-b]pyridine,
- (171) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-(thiophen-2-yl)-2H-pyrazolo[3,4-b]pyridine,
- (182) ethyl 4-(2-bromo-3-nitrophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- 30 (183) ethyl 4-(2-bromo-3-cyanophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
- (189) 4-(2-bromo-3-nitrophenyl)-5-cyano-4,7-dihydro-6-propyl-

2H-pyrazolo[3,4-b]pyridine,
(205) ethyl 2-tert-butoxycarbonyl-4-(2-chlorophenyl)-4,7-dihydro-6-propyl-2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(240) ethyl 4-(2,1,3-benzoxadiazol-4-yl)-6-ethyl-4,7-dihydro-
5 2H-pyrazolo[3,4-b]pyridine-5-carboxylate,
(257) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-hydroxymethyl-2H-pyrazolo[3,4-b]pyridine,
(260) 4-(2-bromo-3-cyanophenyl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine,
10 (264) 4-(2,1,3-benzoxadiazol-4-yl)-5-cyano-4,7-dihydro-6-isopropyl-2H-pyrazolo[3,4-b]pyridine, and
(268) 4-(2-bromo-3-cyanophenyl)-5-cyano-6-cyclopropyl-4,7-dihydro-2H-pyrazolo[3,4-b]pyridine,
a tautomer, an optically active form thereof, a
15 pharmaceutically acceptable salt thereof or a hydrate thereof.

11. A medicament comprising a dihydropyrazolopyridine compound of claim 1, an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof.

20

12. A pharmaceutical composition comprising a dihydropyrazolopyridine compound of claim 1, an optically active form thereof, a pharmaceutically acceptable salt thereof or a hydrate thereof, and a pharmaceutically
25 acceptable additive.

13. A glycogen synthase kinase-3 beta inhibitor comprising a compound selected from the group consisting of a dihydropyrazolopyridine compound of claim 1, an optically
30 active form thereof, a pharmaceutically acceptable salt thereof and a hydrate thereof.

14. The medicament of claim 11, which is used for prevention

and/or treatment of a disease caused by glycogen synthase kinase-3 beta hyperactivity.

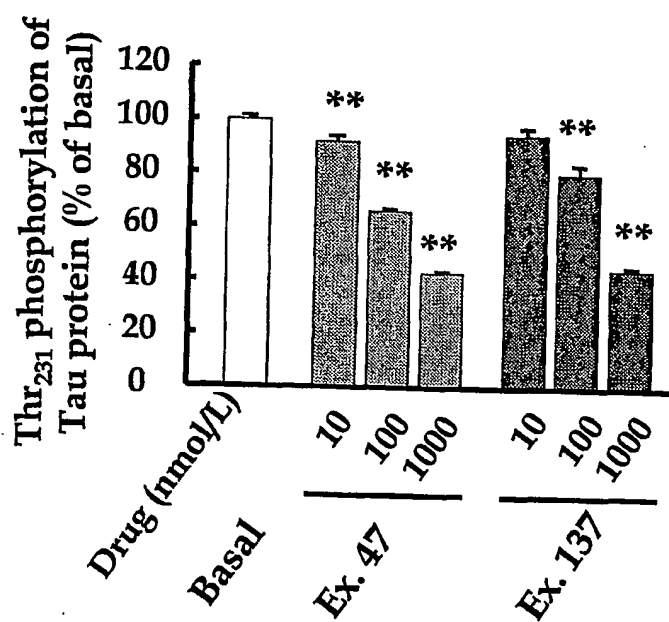
15. The medicament of claim 11, which is used for prevention
5 and/or treatment of a neurodegenerative disease.

16. The medicament of claim 15, wherein the disease is
selected from the group consisting of Alzheimer's disease,
ischemic cerebrovascular disorder, Down's syndrome, cerebral
10 ischemia due to cerebral amyloid angiopathy, progressive
supranuclear paralysis, subacute sclerosing panencephalitic
Parkinsonism, postencephalitic Parkinsonism, boxer's
encephalopathy, Parkinson dementia complex of Guam, Lewy body
disease, Pick's disease, corticobasal degeneration,
15 frontotemporal dementia, AIDS encephalopathy, Huntington's
disease and manic-depressive psychosis.

17. The medicament of claim 11, which is used for prevention
and/or treatment of diabetes and diabetic complications.

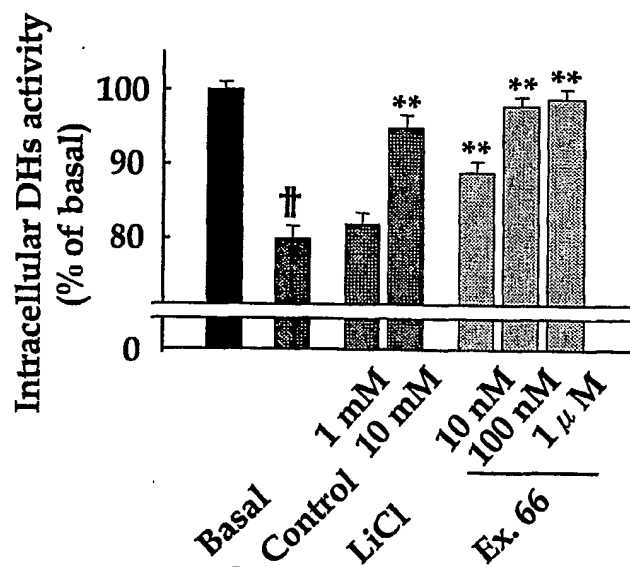
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18. The medicament of claim 11, which is used as an
immunopotentiator.

FIG. 1

Mean \pm S.E.,

** : $p < 0.01$ vs Basal by Dunnett method (n=6)

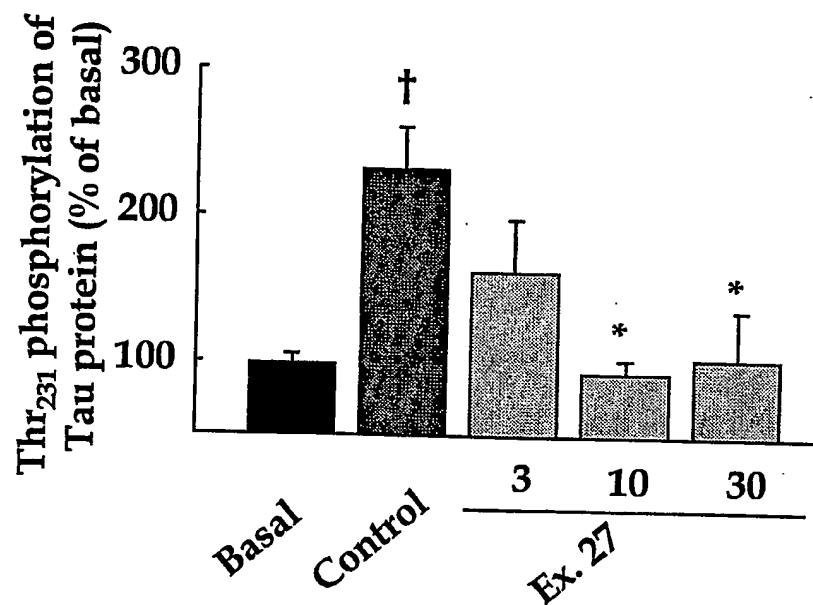
FIG. 2

Mean \pm S.E.,

† : $p < 0.01$ vs Basal by t-test,

*: $p < 0.05$, ** : $p < 0.01$ vs Control by Dunnett method (n=6)

FIG. 3



Mean \pm S.E.,

†: $p < 0.05$ vs Basal by t-test,

*: $p < 0.05$ vs Control by Dunnett method ($n = 3 \sim 5$)